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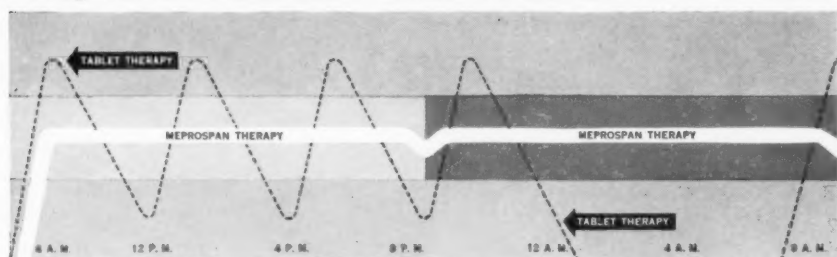
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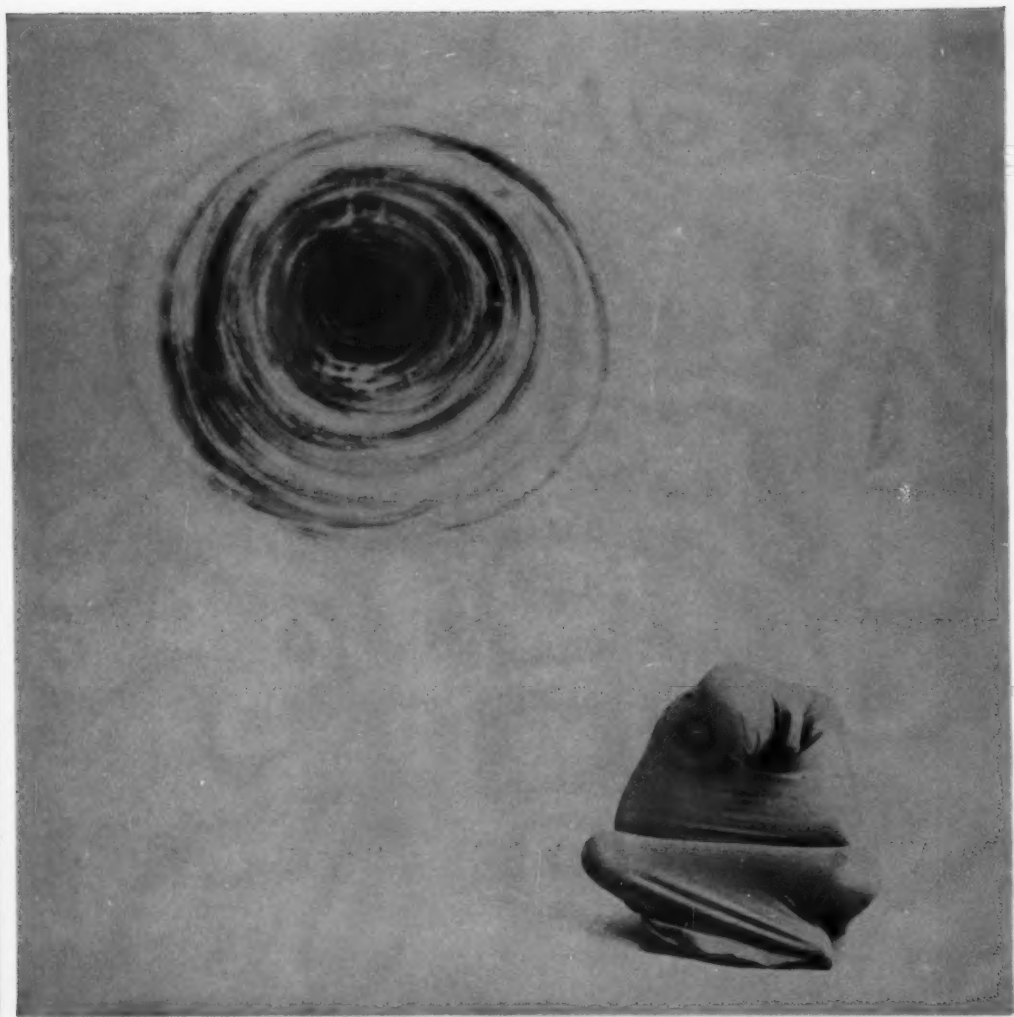
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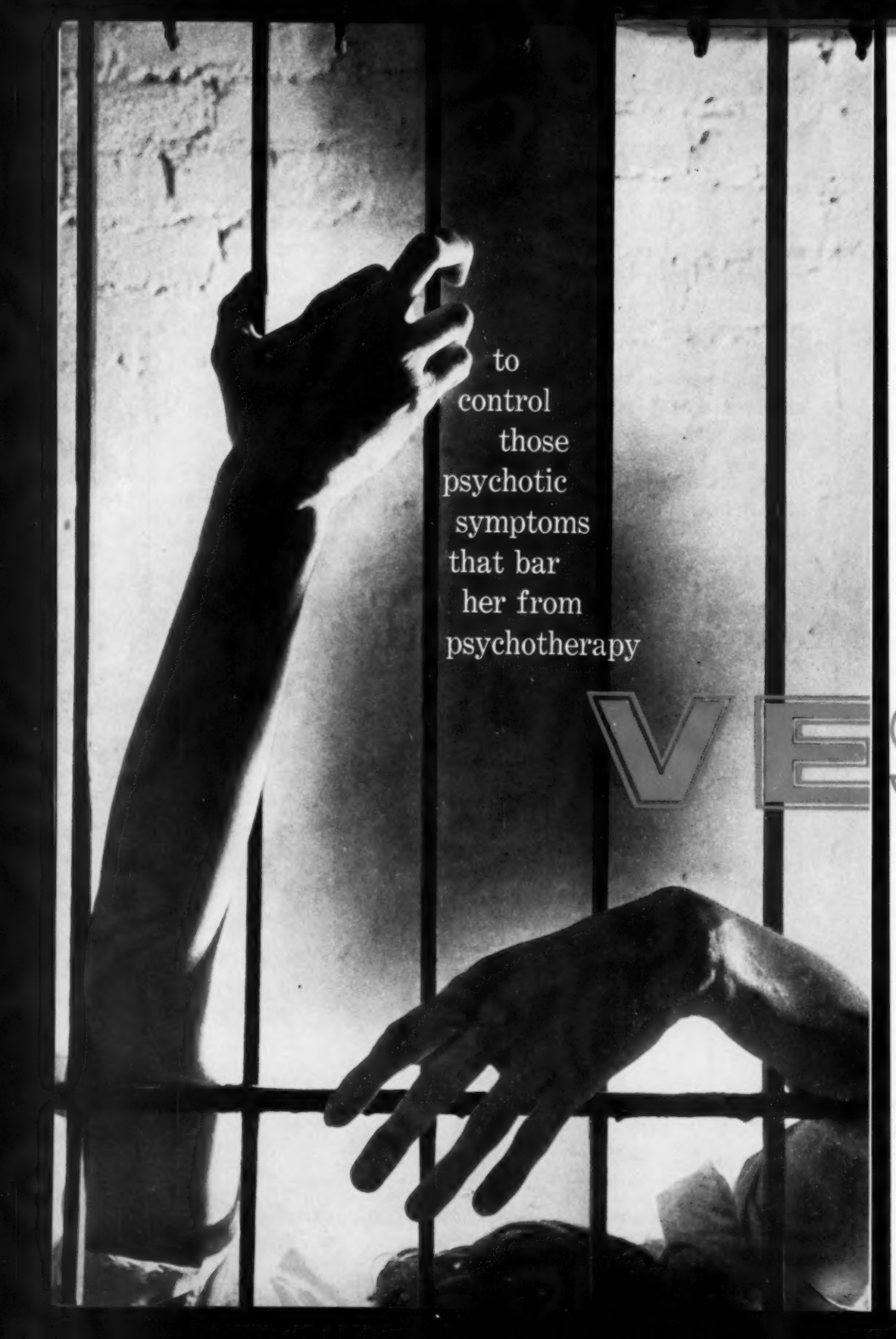
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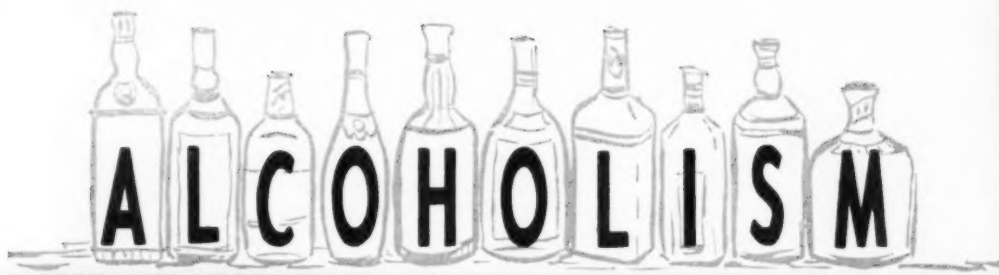
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1. Graffagnino, P. N., Friel, P. B. and Zeller, W. W.: Emotional disorders treated with meprobamate and promazine. Connecticut M. J. 21:1047, Dec. 1957.

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SECTION ON NEUROLOGY

Gliomas of the Optic Nerves

HENRY W. DODGE Jr., M.D.; J. GRAFTON LOVE, M.D.; WINCHELL McK. CRAIG, M.D.;
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The term "glioma of the optic nerve" has been employed commonly to designate a primary tumor arising in the anterior visual pathways (optic nerve, chiasm, and optic tracts). Recently, during a larger study of tumors of the orbit and its contents, it became apparent that a fair proportion of the growths took origin from the optic nerve. It next emerged that primary neoplasms of the optic chiasm and of the optic tracts were at least as common as those of its orbital segment. Moreover, regardless of the point of origin or the extent of the process, these new growths had similar microscopic characteristics and were gliomas rather than neurofibromas. Clinically such a disproportionately large number of them affected children that a congenital origin seemed suggested, and the more-than-occasional associated phenomena of neurofibromatosis (von Recklinghausen's disease) implied that they might even be neoplasms of a hereditary type. These

observations were confirmed in the literature, and it was decided to study, as a group, the cases of this type encountered at the Mayo Clinic with a view to correlating certain clinical and pathologic features in an effort to establish criteria for earlier diagnosis, and to present our ideas concerning the more controversial aspects of adequate treatment for patients afflicted with glioma of the optic nerve.

Review of the Literature

The earliest cases of primary intradural tumors of the optic nerve were reported by Wishart¹ in 1833, and an early study by Middlemore, in 1838, was reported by Parsons.² Parsons also carried out a study of primary intradural tumors and found that separation of these tumors from orbital tumors was first made in 1873 by Goldzieher; that von Graefe in 1864 had attempted to designate criteria of importance for differential diagnosis; that by 1877 Leber had presented a rather rational classification of these tumors, and that in 1902 Byers had compiled a list of 102 cases of primary intradural tumors of the optic nerve, although he had not classified them as to histologic types.

The purpose of Hudson's³ paper in 1912 was to subdivide the available cases in the literature on the basis of critical examination of the records and histologic features. An extensive bibliography of the work previous to 1912 was included in the paper.

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Read before the Section on Nervous and Mental Diseases at the 106th Annual Meeting of the American Medical Association, New York, June 4, 1957.

Section of Neurologic Surgery (Drs. Dodge, Love, and Craig); Section of Surgical Pathology (Dr. Dockerty); Section of Ophthalmology (Dr. Kearns); Section of Roentgenology (Dr. Holman), and Section of Pediatrics (Dr. Hayles), Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

From the subsequent literature on gliomas of the optic nerve, brevity requires that only certain papers be mentioned.

In 1940 Davis⁴ pointed out that primary gliomas of the optic nerve should be carefully segregated on a histologic basis from meningiomas and fibromas which arise from the investing sheath. This had not been done in a literature of some 380 cases, but Davis estimated the ratio of gliomas to meningiomas to be 3:1. He, too, was impressed with the more-than-occasional association of these tumors with von Recklinghausen's disease. The same year Wolff⁵ struck an optimistic note when he observed that after surgical removal the rate of recurrence of histologically verified primary gliomas of the optic nerve was lower than a similar rate for orbital tumors of any other category. Incomplete removal of such gliomas, he found, was sometimes compatible with long life of the patient. He correctly observed and recorded the phenomenon of posterior spread within the substance of the nerve trunk. Invasion of the globe in the opposite direction was, to him, a rare occurrence.

Walsh,⁶ in 1947, took issue with those who expressed the opinion that minor local enucleation was curative for gliomas of the optic nerve. He definitely favored the transfrontal approach of Dandy⁷ (1922) over the time-honored Krönlein operation through the lateral orbital wall.⁸ Suspicion of intracranial extension and the possibility of complete removal were cited as indications for surgical attack by the transfrontal method, and direct inspection of the chiasmal regions and the contralateral optic nerve was cited as an added advantage of this method.

In 1950 Bucy, Russell, and Whitsell⁹ found that two-thirds of some 400 "optic nerve tumors" were in fact primary gliomas of the optic nerve. They felt that the low incidence of reported recurrence after surgical removal did not reflect the fact that removal was complete as much as it reflected the short term of follow-up studies.

Such studies, in their opinion, were meaningless when conducted on neoplasms whose life histories are measured in terms of decades.

Cohen¹⁰ was not convinced that intracranial extension should be ruled out on the basis of clinical or roentgenologic evidence. The subject of the transcranial approach to orbital tumors was reviewed by Love and Dodge¹¹ in 1953.

In an interesting analysis of the entire subject in 1954, Marshall¹² perhaps overestimated (16.4%) the associated incidence of von Recklinghausen's disease with gliomas of the optic nerve. His article tends to give the impression that the occurrence of skin blemishes was accepted as evidence of neurofibromatosis.

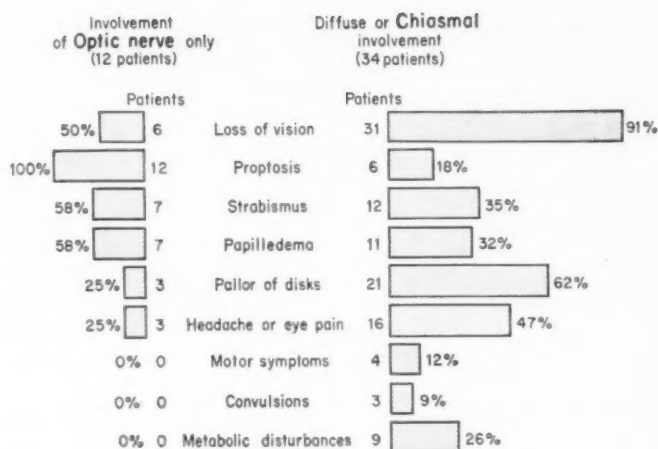
In 1956 a significant and well-written article by Taveras, Mount, and Wood¹³ was published. They reported on irradiation therapy of primary gliomas of the optic nerve and indicated that excellent results may be achieved by this method. It is interesting to note, however, that in a number of cases in which patients were benefited by such therapy the type of lesion had not been verified by surgical biopsy. Therefore final judgment of this particular form of therapy must be delayed, especially since the follow-up studies on their series were so short.

These articles reviewed from the literature offer only a brief résumé of the many outstanding contributions in a field that boasts voluminous documentation. They do contain the necessary bibliography for the interested reader to follow, however, should he wish to delve more deeply into the history of this particular lesion.

Materials and Methods

In reviewing the cases of gliomas encountered at the Clinic, the decision was made to include only those instances of tumor primary in the optic apparatus from the emergence of its tracts from the optic globe to their entrance into the substance of the brain. Brain tumors with secondary involvement of the optic tracts were deleted accordingly. It was next agreed to qualify for inclusion only those cases in which positive surgical

Fig. 1.—Distribution of patients having gliomas of optic nerve only and those having diffuse or chiasmal involvement at time of diagnosis according to presenting symptoms and signs.



or necropsy material was available for study. These criteria were confirmed in 46 cases over a 41-year period, from 1915 to 1955. These cases were analyzed and form the basis of this report. During this same period more than 6000 intracranial tumors have been encountered at the Clinic.

For the pathologic studies discussed later, old slides were reviewed, and new slides were made from wet tissue, which had been preserved in practically all instances. Sections were stained with hematoxylin and eosin after impregnation with paraffin; special impregnation mounts were prepared as necessary. In all, some 400 sections were assembled.

The 46 patients in this series were divided into two groups on the basis of surgical and pathologic observations of the lesion. Group 1 included 12 patients, each of whom was found to have a glioma limited to the optic nerve at the time of operation. Group 2 included the other 34 patients, each of whom had a more diffuse glioma that involved the chiasm or optic tracts. It is to be emphasized that the division of these cases was on the basis of pathologic findings rather than on clinical grounds, since a number of the patients who appeared to have lesions of the optic nerve with unilateral loss of vision and proptosis of one eye only were found at exploration actually to have more diffuse involvement.

Group 1: Glioma of the Optic Nerve

Proptosis.—The most outstanding finding in this group (Fig. 1), of 12 patients, was proptosis. Each of the 12 patients had proptosis; most of them gave it as their initial complaint, and it was for proptosis that they had sought help. It appeared to be a forward

protrusion without vertical or lateral displacement of the globe, as would be expected with a lesion of the optic nerve. In most cases it was moderate in degree, the globe being definitely prominent yet not extremely exophthalmic, as it commonly is when proptosis is associated with other conditions, such as diffuse malignant disease of the orbit. No exact average measurements of the degree of proptosis could be obtained, since a number of the patients were infants and children too young to cooperate for such measurement.

Loss of Vision.—Six of the twelve patients in Group 1 had loss of vision of the affected eye. The young age of some of the patients often made visual testing difficult, if not impossible. Only two patients were known to have normal visual acuity in each eye, and both had a central acuity of 20/20 in each eye. It seems strange that a glioma of the nerve capable of producing proptosis would not give rise to loss of vision, but perhaps this is analogous to the infiltration of certain types of brain tumors that likewise seem to infiltrate vital structures without giving early rise to impairment of conduction. Four patients had either complete blindness of the eye or only faint light perception. The young age of these patients usually prevents testing of the fields with the perimeter and

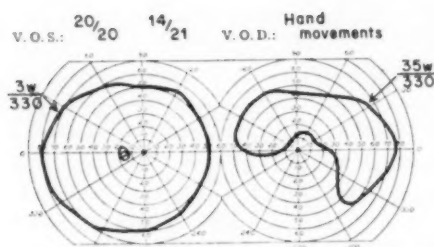


Fig. 2.—Perimetric fields of 13-year-old girl with glioma of right optic nerve.

tangent screen, but, if possible, a prechiasmal type of loss is to be expected, with, of course, a normal field in the opposite eye (Fig. 2).

Strabismus.—Strabismus was a frequent finding, and in several patients it was the initial abnormality noted by the parents. In the majority of cases the strabismus was merely a reflection of the blindness of the eye and consisted of esotropia. Several patients seemed to have some limitation of motion of the proptosed eye, and the deviation of the eye appeared to be due to mechanical factors secondary to proptosis. In none of the cases was strabismus thought to be due to involvement of a cranial nerve. Nystagmus, likewise, was not present in any of these patients.

Ophthalmoscopic Findings.—Of the 12 patients, 7 were found to have unilateral papilledema on the affected side. The papilledema varied in degree but usually tended to be severe. In several of the patients it was noted that not only was papilledema present but the entire posterior pole of the fundus appeared to be elevated. Such a finding is usually pathognomonic of orbital tumor. None of the patients was thought to have gliomatous invasion of the optic nerve head itself.

Three patients had pallor of the disk on the affected side. The pallor varied from minimal, in one case, to an intense whiteness, in another. It appeared to be the pallor of simple optic atrophy, and not that of atrophy secondary to previous papilledema, in all three cases.

Of the two remaining patients, without papilledema or pallor, one had the aforementioned "pushed-in" appearance of the posterior pole, and the other had a cataract which prevented a view of the fundus. Therefore all patients in whom the fundus could be observed had ophthalmoscopic changes, as well as proptosis.

Age and Sex.—The ages of the 12 patients ranged from 2 to 21 years, most patients being young children. The average age was 8.8 years, and as a whole the patients in Group 1 tended to be younger than those of the chiasmal group.

Ten of the twelve patients were female, in accordance with the generally accepted opinion that gliomas of the optic nerve occur more commonly among females than among males.

Group 2: Glioma of the Chiasm or Optic Tract

Loss of Vision.—Loss of vision, usually bilateral, was the outstanding symptom of this group of 34 patients (Fig. 1). It was the symptom for which the majority of patients in this group sought help.

Of the 34 patients of this group, 31 were found to have some visual loss of one or both eyes. Two of the three patients in whom loss of vision could not be confirmed were too young, one being 2 months and the other 2 years of age. The other patient, an 18-year-old youth, had normal central acuity and normal visual fields with both the perimeter and the tangent screen. This case, like the two cases of the optic nerve group, serves to illustrate that, although the occurrence is unusual, a glioma may be present and produce symptoms (4Δ of papilledema of each disk in this case) without giving rise to loss of vision.

In Group 2, bilateral loss of vision was found in 23 patients, the field defects usually being of a bitemporal or incongruous homonymous nature. In 9 of the 23 patients the defects were of a type which might be termed "typical bitemporal defects," an example of which is shown in

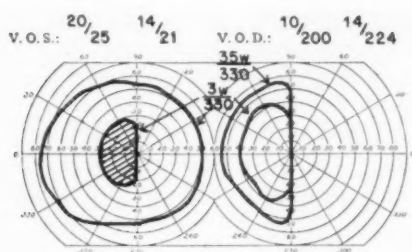


Fig. 3.—Perimetric fields of 34-year-old man with typical bitemporal defects of glioma of optic chiasm.

Figure 3. As can be seen, there is little that distinguishes these fields from those of any other chiasmal lesion. In our experience it has been impossible to differentiate the bitemporal defects of various chiasmal lesions from one another on the basis of visual fields alone with any degree of accuracy.

Of the 34 patients, 8 had only unilateral loss of vision, although, again, the young age of some of the patients may have prevented detection of a slight loss of vision in the better eye. The fields do not differ significantly from the fields of a patient with a lesion limited to the optic nerve only.

Proptosis.—Six patients had proptosis and were found to have involvement of the intracranial visual apparatus. Five of the six had unilateral symptoms, making them indistinguishable clinically from the patients with involvement of the optic nerve only.

Ophthalmoscopic Findings.—Pallor of the disks was present in 21 of the 34 patients and was bilateral in all but 4 cases. The pallor in all cases was generalized pallor of the entire disk, and, like that of patients having lesions of the optic nerve, it appeared to be the pallor of simple optic atrophy rather than that following papilledema.

Of the 34 patients, 11 had papilledema (32%), 5 having unilateral and 6 bilateral edema. It is interesting to note that papilledema occurred in 58% of Group 1, the optic nerve group, and pallor in 25%; but the opposite was true of Group 2, the

chiasmal group, in which pallor occurred in 62% and papilledema in 32%.

Strabismus.—Patients in Group 2, with blind or near-blind eyes, had strabismus, as did the patients in Group 1, but none of the patients in either group had any evidence of involvement of a cranial nerve producing palsy of extraocular muscles. Three patients had a searching type of nystagmus. This occurred only in the younger patients and should indicate that the onset of visual loss occurred early in life.

Age and Sex.—Both age and sex of patients in this group contrasted sharply with those of patients having glioma of the optic nerve. In general the patients in Group 2 were older than the patients in Group 1; several patients were in their 30's, and one patient was 46 years of age. The average age for the entire group was 14 years.

We were surprised to find that there were more males than females in Group 2; this was contrary to the usual belief that females are more commonly affected with glioma of the chiasm. There were 19 male to 15 female patients, statistically suggesting that both sexes are about as frequently affected when the glioma involves the chiasm.

Roentgenologic Aspects

A further study was made of the 46 proved cases of glioma of the optic nerve or of the optic chiasm or of both to evaluate any recognizable changes in standard roentgenographic projections of the head and of the optic foramina, as demonstrated in the Rhese position. At the Clinic, in the Section of Roentgenology, it is considered that an adequate study of the orbit might include (1) a routine roentgenogram of the skull with stereoscopic lateral views, (2) views of the optic foramina, (3) views with the patient in the Caldwell position, (4) views with the patient in the Waters position, and (5) occasional stereoscopic views of the base of the skull. In a few cases more details of the orbit may be

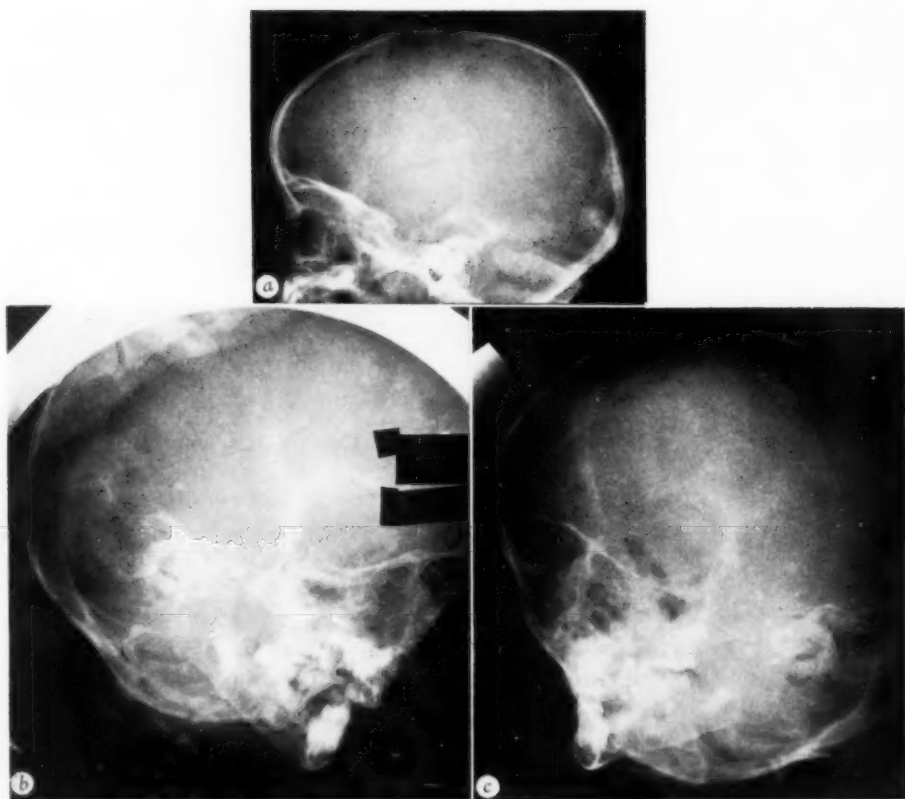


Fig. 4.—(a) Lateral roentgenogram of skull to demonstrate normal "infantile type" of sphenoid. (b) and (c) Roentgenograms of skull taken with patient in Rhese position, showing that left optic foramen (b) is approximately four times the caliber of the right (c).

obtained by tomograms. In our opinion, adequate information can be obtained in most cases by routine views of the skull and optic foramina.

Routine roentgenograms of the head of 12 patients in each of whom only one optic nerve was known to be involved did not show evidence of abnormality. In Group 1, eight patients had roentgenograms made while in the Rhese position, and in seven gross enlargement of the optic foramen was evident on the affected side (Fig. 4). In the eighth patient the tumor was entirely intraorbital. One additional patient, a girl 2 years of age, showed enlargement of both optic foramina and marked concavity of the chiasmatic sulcus region of the sphenoid. Surgical exploration revealed a gli-

oma of the right optic nerve. Involvement of the left optic nerve or chiasm was not seen at this time.

In only 4 of the 34 patients having gliomas which involved the optic chiasm were roentgenograms of the skull considered to be entirely normal. The region of the chiasmatic sulcus showed a large concave depression in eight cases and a shallower depression in an additional eight. Because this region usually undergoes a rather marked alteration in shape during development from the infantile to the adult form, it is suggested that a slow-growing tumor originating in this region at an early age might be responsible for the concave outline of the chiasmatic sulcus region. This shape is not pathognomonic of such a tumor, for



Figure 5

Fig. 5.—Lateral view of skull, illustrating marked concavity of region of chiasmatic groove and decalcification of anterior clinoid processes.



Figure 6

Fig. 6.—Reproduction of diagnostic ventriculogram to show obstruction of foramen of Monro

with symmetrical hydrocephalus of lateral ventricles and upward convexity of floor of anterior horns of ventricles. To be noted also are marked changes in sella turcica, chiasmatic groove, and posterior clinoid processes.

it is known to be present occasionally in normal persons and more frequently in patients having conditions affecting growth and development, such as neurofibromatosis, hypothyroidism, Mongolism, rickets, skeletal dysplasia, and dystrophies. However, this outline of the sphenoid, when accompanied by enlargement of one or both optic foramina or in the presence of appropriate visual disturbances, should suggest the possibility of glioma of the optic chiasm (Fig. 5).

Six patients of Group 2 had roentgenologic evidence of increased intracranial pressure. In five cases a definite separation of the cranial sutures was noted. One of these patients, as well as one other, also had an abnormal prominence of the convolutional impressions of the vault. There was no instance of roentgenologically demonstrable tumor calcification in this entire series.

Pneumoencephalography was carried out in three cases and ventriculography in four. All of the pneumoencephalographic examinations demonstrated obliteration of the cisterna chiasmatis and lamina terminalis, posterior dislocation of the anterior portion of the third ventricle, and an outline of part

of the suprasellar tumor in the cisterna interpeduncularis. There was also a slight upward bulging of the floor of the anterior horn of each lateral ventricle.

Ventriculography showed marked obstruction of the foramina of Monro in three patients and a similar, although incomplete, obstruction in one. The lateral ventricles consequently were dilated and showed an upward convexity of the floor of the anterior horns (Fig. 6). In the case of incomplete obstruction, the third ventricle was compressed from an anteroinferior direction.

Only two cerebral angiograms were attempted, and both were considered to be normal. In one patient, a 46-year-old woman, the tumor was located entirely within the bony orbit. The second patient was a 34-year-old man who had a suprasellar tumor with associated shortening and decalcification of the dorsum sellae. Convincing evidence of vessel displacement was not noted.

Endocrine Disturbances

Among the 46 patients of this study, 9 manifested evidence of disturbed endocrine function before the diagnosis of glioma of

the optic nerve was established. In each of these nine patients the tumor rose within the cranial cavity.

No specific pattern of growth and development or endocrine abnormality is associated with tumors arising in the optic nerve. These tumors apparently produce endocrine symptoms by virtue of pressure or direct extension into the area of the hypothalamus or the pituitary gland. Increased intracranial pressure is almost invariably present in patients with abnormal endocrine function.

The nine patients considered to have evidence of endocrine disturbance were found to have precocious puberty, obesity, mental retardation, and pituitary insufficiency. Other evidences of endocrine dysfunction were found to be hypogonadism and eunuchoid habitus. In one boy gynecomastia developed. The eunuchoidism noted in these patients was characterized by increased height with thin arms, legs, and hands, underdeveloped genitalia, and poorly developed or absent secondary sex characteristics.

Pathologic Aspects

Pathologically, from the gross and microscopic standpoints, it was convenient to divide the types of tumors as follows: Type A, tumors of the optic nerve, 12 cases; Type B, tumors of the optic chiasm, 14 cases, and Type C, "tractal," or diffuse, tumors, 20 cases.

All 12 tumors of Type A were unilateral. Encapsulation was good in the nine instances in which proximal and distal section of the optic nerve had been performed, with stumps of the latter submitted for examination along with the intact tumor. In the three remaining patients piecemeal intracapsular removal had been dictated as the procedure of choice because of the type of operative approach, the large size of the tumor, or the presence of dural adhesions. Four of the intact tumors were globular, and four were lozenge-shaped. The greatest diameter of the former was 3 cm., and

the longest dimension of the latter was 4.5 cm. The most diminutive of the tumors was a spherical nodule 1.5 cm. in diameter affecting the midsection of the left optic nerve.

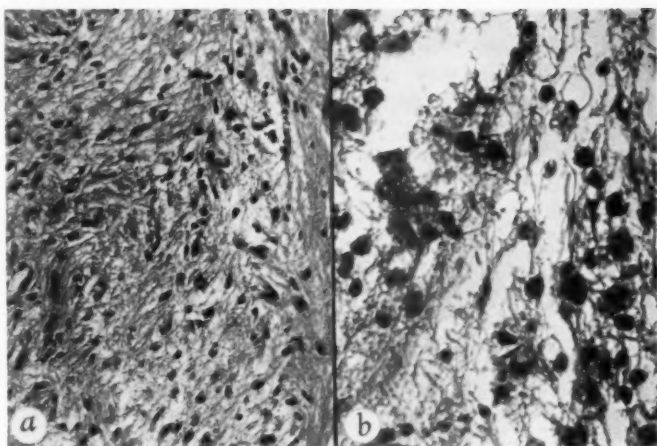
In five instances placement of the tumor with respect to the nerve was more or less symmetric, and in three the nerve seemed to pursue a tangential course in relation to the tumor. Distal spread toward the globe was not found, but in three instances proximal intraneural or perineural involvement was demonstrated by fresh frozen sections of resected nerve stumps. Further sacrifice of tissue was required in these cases. Comparable examination was not possible in the three instances in which piecemeal removal of the tumor had been accomplished. No residual tumor was found at the time of these secondary operations.

Microscopically, all 12 neoplasms were astrocytomas, although in 2 a scattering of oligodendrocyte-like cells was noted. Nine of the growths were composed of coarse fibers, with a preponderance of elongated bipolar cells with thick processes. The designation "fibrous astrocytoma" seemed to be a reasonable one for these tumors. In the remaining three instances the processes were fibrillar rather than coarse, and occasional protoplasmic astrocytes with retracted cytoplasm were featured (Fig. 7a and b).

By the Kernohan method of grading, only 1 of the 12 tumors was considered to be an active neoplasm (Grade 3), by virtue of its containing fair numbers of mitotic spindles. Seven of the remaining eleven tumors were Grade 1 lesions, and the remainder were Grade 2 astrocytomas. In four tumors, somewhat swollen, but otherwise intact, filaments of the optic nerve were observed coursing through the neoplasm (Fig. 8a and b).

Cytoid bodies were present in seven tumors, and in one of these it was difficult to be sure of the absence of ganglion cells (congenital anomaly?). About the growths, the epineural space of Disse exhibited in-

Fig. 7.—(a) Low-grade astrocytoma, fibrous type (usual) with coarse bipolar cells. Hematoxylin and eosin; reduced to 96% of mag. $\times 200$. (b) Finely fibrillar type (25%) with filamentous glia. Several "gemistocytic" astrocytes appear as swollen forms. Hematoxylin and eosin; reduced to 96% of mag. $\times 400$.



vasion by neoplastic tissue in five, and in two there was extension beyond into the interstices of the dura. A reactive proliferation of this layer and of the arachnoid likewise was observed in 10 cases.

Ancillary pathologic changes included the presence of associated cutaneous pigmentation in three patients, but biopsy was not carried out to ascertain the nature of these blemishes. In one patient in this group an intracranial neoplasm developed subsequently, but whether this represented extension of the original glioma of the optic

nerve or an independent growth could not be ascertained.

Gross material received from patients with Type B lesions differed from that of the preceding group in that it was practically always delivered piecemeal. In six patients biopsy only had been done, and in eight patients doubt existed that anything like complete removal of the tumor had been accomplished.

In one instance a fibrous astrocytoma involving the chiasm and left optic nerve was found at necropsy. The patient, a

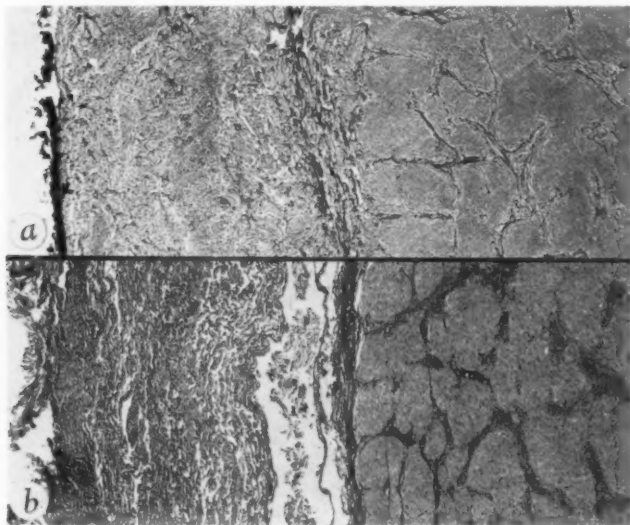


Fig. 8.—(a) Astrocytoma, Grade 2, showing spread within sheath of optic nerve. (b) Astrocytoma, Grade 1, with dural and arachnoidal thickening contributing to bulk of tumor. Hematoxylin and eosin; $\times 40$.

2-year-old spastic infant, had died after cerebral decompression for unlocalized brain tumor. Neoplastic tissue varied in aggregate from tiny specimens to those that measured $3.5 \times 2.5 \times 2$ cm. In the laboratory we were rarely ever able to identify normal elements of optic nerve in this tissue. One of the tumors was cystic, and the remainder were solid; otherwise they possessed the gross characteristics outlined for Type A lesions.

Microscopically, 1 of the neoplasms was a Grade 3 oligodendroglioma; the remaining 13, all astrocytomas, were perhaps a little more active than the Type A lesions, and increased vascularity was prominent in 8. By the Kernohan method of grading, six lesions were of Grade 1, five were of Grade 2, and two were of Grade 3. Disse's space, adherence to the arachnoid and dura, and reactive proliferation of elements on the arachnoid and dura were observed in these lesions, as they were in the Type A lesions. Cytoid bodies were identified in eight specimens.

The most extensive nature of these chiasmal lesions was reflected in the comparatively poor results of surgical and roentgenologic treatment. Five patients have been reexamined recently for the first time since operation, and follow-up studies on them are meaningless. Of the remaining nine, three died with clinical evidence of extension into the brain, and such extension was evident at necropsy in one other case. An additional three patients are suffering from the effects of obstructive hydrocephalus at the time this paper is being written. Only two patients in this group have stigmas which could be interpreted as indicating possible von Recklinghausen's disease.

Of the 20 Type C lesions, 17 were bilateral with respect to the chiasm and tracts, and 3 showed predominantly unilateral involvement. Anterior extension of the growths into the optic nerve was believed to exist in most instances, but actual proof of such extension was afforded by biopsy in two cases only. In one of these, intra-

capsular enucleation of a glioma of the left optic nerve had been performed in 1951 through an orbital approach. Three years later a recurrent lesion, the size of a golf ball, was found intracranially. Posteriorly the degree of spread was such that total removal was impossible. Indeed, in only five instances was subtotal removal attempted, the lesions being cystic in two instances and solid in three.

Obstruction of the third ventricle from encroachment on it by neoplastic tissue was recorded in seven instances, either at operation or at necropsy. In three patients seen prior to 1930, the existence of such obstruction had suggested the presence of a lesion in the posterior fossa, the gliomas of the optic nerve being accidental findings at necropsy. This complication developed in three additional patients months to years after operation. The coexistence in one patient of a tumor of the cerebellopontine angle clinically, four years after the appearance of the lesion under discussion, emphasizes the occasional association of true and verified neurofibromatosis (von Recklinghausen's disease) with primary tumors of the optic nerves. Three other patients in this group of 20 had cutaneous stigmas of neurofibromatosis (pigmented spots). Their identity with true café au lait spots implies a degree of personal bias, however.

Gross pathologic material available for study in Type C lesions consisted of tiny specimens in 10 cases, necropsy material alone in 3 cases, measurable products of subtotal resection in 4 cases, and surgical plus necropsy specimens in the remaining 3 cases.

Fifteen of the growths were astrocytomas, Grade 1, predominantly fibrous in type. In two of these the presence of ganglion cells indicated an origin from heterotopic tissue, since these elements are not normally found in the extracortical reaches of the visual apparatus. In one of these two cases, and in another in which ganglion cells were not found, the presence of scattered oligodendrocytes was noted. Micro-

scopically, seven of these Grade 1 astrocytomas were rather vascular.

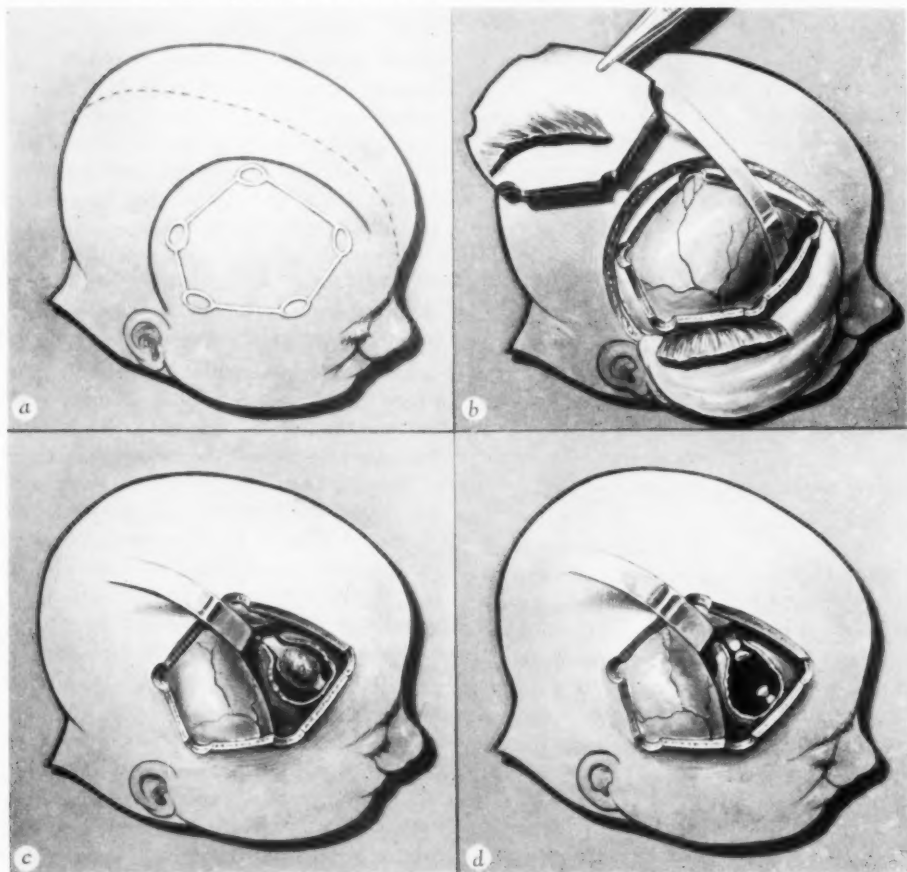
Four of the lesions exhibited degrees of cellular atypism, increased cellularity, and other features which justified their designation as astrocytomas Grade 2. Vascularity was prominent in them, as was the presence of increased numbers of protoplasmic astrocytes. Central liquefaction was a feature in two of these four tumors. The remaining lesion was a Grade 3 astrocytoma with mitotic figures and large numbers of protoplasmic astrocytes. Cytooid bodies were noted in 10 of the 20 tumors of Type C.

However, the nature of the available material of tumors in this category was not such as to permit assessment of the degree of extraneural involvement, arachnoidal proliferation, and so forth. By the same token, as was previously mentioned, it was practically impossible to establish just where the tumors in this group had their beginning.

Treatment

To our way of thinking, the treatment for primary tumors affecting the anterior visual pathways is surgical. Our experience

Fig. 9.—(a) Scalp incision and bone flap outlined for right transfrontal craniotomy to explore right orbit, optic nerve, and chiasm. (b) Scalp turned down and bone flap removed. Surgeon is beginning to retract dura covering orbit. (c) Brain retracted, roof of right orbit partially removed, and glioma of optic nerve exposed. (d) Glioma of optic nerve completely resected and cut ends of nerve visualized.



has led us to favor the transcranial attack. However, the choice of surgical approach to the orbit and optic nerves should be the result of joint consultation between the ophthalmologist and the neurosurgeon. In previous reports we have presented our impressions of the indications for transcranial operation for orbital tumors, progressive exophthalmos, and so forth.¹¹

Contrast orbitography with air or other media (direct injection into Tenon's capsule) should be added to the previously mentioned diagnostic aids of carotid angiography, pneumoencephalography, and ventriculography used by the roentgenologist and the neurosurgeon. However, increased experience shows that a carefully taken history and close observation and examination of the patient often are as helpful as any particular mechanical test.

The commonest transcranial approach to the orbit and optic nerve is via frontal craniotomy (Fig. 9*a, b, c, and d*). Simultaneous exploration of both orbits and visualization of both optic nerves may be achieved by using a Souttar type of concealed scalp incision and a bifrontal craniotomy. Various modifications of this approach have been described.

Gliomas limited to one nerve can be excised completely. More diffuse tumors of the optic nerve and chiasm or tract can be surgically verified and resected to varying degrees by this type of approach. If necessary, exploration of the sella turcica and pituitary gland can be achieved at the same time.

The risk associated with transcranial operation on the anterior optic pathways has been greatly minimized by newer operative and anesthetic techniques. Surgical hypotension, improved hemostatic materials, minute-to-minute control of body fluid and blood requirements, regulation of body temperature, and intratracheal combined anesthesia affording high concentration of oxygen to the lungs all aid in the safe maintenance of the patient. In addition to these aids, the use of an indwelling spinal

catheter for removal and replacement of cerebrospinal fluid to allow the frontal lobe of the brain to fall back minimizes the necessity for retraction and affords excellent visualization. The increasing familiarity of neurosurgeons with the contents of the orbit, and their knowledge of local anatomy, gained through interventions to explore the sella turcica and frontal lobes for other purposes, have helped to facilitate surgical maneuvers in this particular region of the head.

Experience with gliomas of the anterior visual pathways and other orbital lesions has indicated certain advantages of transcranial operations to both the patient and the surgeon. These advantages are as follows: (1) excellent direct visualization of the orbit and anterior visual pathways; (2) more adequate control of hemorrhage by means other than pressure tamponade; (3) lessened need for blind palpatory exploration of orbital contents; (4) added postoperative decompression of orbital contents; (5) opportunity for exploration of orbital contents and intracranial portions of the optic nerve simultaneously; (6) bilateral visualization of the anterior optic pathways if necessary; (7) hidden intrahairline operative scalp incision, and (8) the chance for total removal of certain of these tumors.

In the main, the patient's inherent reservation about craniotomy has been the chief contraindication to the utilization of the transcranial approach to the anterior visual pathways. Seemingly, however, because of the chance for complete removal and cure of certain gliomas of the optic nerves and the lessened postoperative cosmetic defect, the physician when confronted with such a problem might well consider the merits of the transcranial approach when dealing with tumors of the optic nerve (Tables 1 and 2).

In certain cases, orbitoplasty¹⁴ has been performed after exploration of the orbit, and a small piece of stainless steel has been used to cover the decompression in the orbital plate. Subsequent pulsation of the

GLIOMAS OF OPTIC NERVES

TABLE 1.—Results of Surgical Resection for Gliomas of Optic Nerve (Twelve Patients)

Years After Operation	Patients Living
1	2
3	1
6	1
8	1
10	1
12	1
14	1
15	1
22	1
Total	11 *

* One patient died of unrelated brain tumor four years after operation.

globe may thus be avoided in the rare case in which it has annoyed the patient. Orbitoplasty of this type is often helpful if at some subsequent time exenteration of the orbit is undertaken, for it prevents the ophthalmic surgeon from entering the undersurface of the brain.

The care of the eye after transcranial approach to the orbit or anterior visual pathway has been the province of the ophthalmologist, and the need for blepharorrhaphy has been extremely uncommon.

Removal of the ocular globe has not been deemed necessary, for several reasons. Primarily, invasion of the optic nerve head is rare, and intraneural spread is commonly toward the optic chiasm. Secondly, the patient's own globe, even with a blind eye, is generally more satisfactory than any prosthesis. If intraocular invasion is suspected after resection of an optic nerve, the globe can always be removed at that time, but in most cases removal will prove unnecessary.

X-ray treatment of gliomas of the anterior visual pathways has been difficult to evaluate. This is true because the natural life of the tumor may be prolonged, even if the lesion has been only partially resected surgically or biopsy alone carried out, followed by irradiation, vitiating the evaluation of any particular method of treatment.

Roentgen therapy of those lesions affecting the anterior visual pathways, presumed to be gliomas, and surgically unverified, of necessity must leave a hiatus of conjecture in our knowledge.

Dodge et al.

TABLE 2.—Results of Partial Resection or Biopsy for Diffuse Chiasmal Involvement (Thirty-Four Patients *)

Years After Operation	Number of Patients	
	Living	Dead
1	2	8
2	4	1
3	3	2
4	1	1
5	1	1
6	2	0
12	5	0
15	2	0
Total	20	13

* One patient was not traced.

The recent work of Taveras and his collaborators¹³ suggested x-ray therapy to be quite beneficial. Our own experience with x-ray therapy as the sole means of treatment is too small to allow evaluation.

Comment

Tumors of the pons, the cerebellum, and the optic apparatus share a rather marked predilection for development during childhood years. This fact is brought into prominence by the present study, in which 33 of the 46 patients were children. In many of them the evidence points rather strongly to a congenital origin of their tumors. Moreover, like pontine tumors of childhood, tumors of the optic nerve are practically all astrocytomas; like their cerebellar counterparts, the neoplasms are of a low order of malignancy. It is interesting that, by comparison, the majority of other supratentorial astrocytomas are fairly anaplastic neoplasms. Especially is this true in the case of patients more than 60 years of age, in whom practically all astrocytomas are lesions of Grade 3 or Grade 4 by the Kernohan method of classification.

The occurrence of ganglion cells in several of the tumors raised the question of whether or not the tumors originated from heterotopic brain tissue, since ganglion cells normally do not form after birth and normally do not occur within the extracerebral portions of the optic tracts. One tumor contained ganglion cells in such numbers as to warrant designation as a neuroastrocytoma (ganglioneuroma). The presence of

pink-staining cytoïd bodies containing nuclear debris was easy to confuse with ganglion cells.

Under ordinary circumstances oligodendrocytes occur in satellite clusters associated with ganglion cells. It is not surprising, therefore, that only one tumor could be classified as an oligodendroglioma. In only a few additional instances were oligodendroglial cells observed. We cannot subscribe to the notion of Lundberg¹⁵ that tumors of the optic nerve are basically oligodendrogliomas. Eosinophilic "cytoïd" bodies, occurring as small dots within the cytoplasm of neoplastic cells or lying free as relatively large globular masses, appeared to represent the end-products of a degenerative process and did not appear to offer anything in a diagnostic way. They are fairly regularly observed in astrocytomas occurring elsewhere, as well as in non-neoplastic lesions of the brain. As mentioned previously, they are apt at times to be confused with ganglion cells.

With respect to the spread of gliomas of the optic nerve, one is first impressed with their tendency to permeate the substance of the nerve, especially in a proximal direction. With tumors which are grossly confined to the optic nerve and which appear to be readily resectable, microscopic examination of the proximal cut end of the optic nerve often reveals the presence of unsuspected involvement. Such a finding requires that the surgeon remove further segments until tumor-free tissue is obtained. Such involvement in regions of the optic nerve proximal to zones which are removable via the orbital approach is an argument favoring the broader exposure provided by transfrontal craniotomy in handling these tumors.

Distal spread of the tumors with invasion of the globe was, in our experience, a rare event, and not per se a reasonable indication for exenteration of the orbital contents. Proximal extension of gliomas of the optic nerve via the sheath space, while occurring in perhaps half of the cases, was never

observed to the same extent as the more dangerous spread within the nerve itself. At times extension in the sheath can be distinguished from the innocent, but cellular, proliferations of the enveloping dura and arachnoid only by means of special stains.

The thesis that gliomas of the optic nerve are but part of a complex which includes generalized neurofibromatosis and cerebellar and other tumors did not find confirmation in our study. Of our 46 patients, 9 displayed skin blemishes, which varied all the way from cutaneous hemangiomas to pigmented moles. In six patients they were called *café au lait* spots; yet in only one was there microscopic proof of an associated neurofibroma. One additional patient had a cerebellar astrocytoma successfully treated by surgical removal four years after extirpation of a glioma of the optic nerve. All "brain tumors" developing in the remaining patients gave symptoms of hydrocephalus from the anticipated or demonstrated involvement of the third ventricle secondary to proximal progression of lesions in the optic tract.

Summary

This report is concerned with 46 surgically verified primary gliomas of the anterior visual pathways (familiarily known as gliomas of the optic nerve) encountered at the Mayo Clinic between 1915 and 1955. A brief review of the pertinent literature is included. From the standpoint of presenting ophthalmologic symptoms, these 46 patients could be analyzed in two groups: a group of 12 patients who had gliomas of the optic nerve and a group of 34 patients who had a diffuse or chiasmal type of glioma. Proptosis was the outstanding finding in patients having tumors of the optic nerve, and bilateral loss of vision, in 23 of 34 patients having more diffuse, or chiasmal, gliomas.

Gross and microscopic examination of gliomas of the optic nerve revealed most of them to be low-grade astrocytomas, with

an occasional oligodendroglioma and ganglioneuroma. All types exhibited tendencies to spread proximally, that is, toward the optic chiasm, along the nerve and its sheath, sometimes with a proliferative reaction in the sheath that added to the bulk of the tumor. This was true especially in orbital examples.

A congenital relation is suggested, since 33 of the 46 patients were children.

These studies indicate an excellent prognosis for unilateral lesions of the optic nerve, with so-called cure following total removal. The more diffuse tumors, which involved the optic chiasm and tracts, carried a less favorable prognosis. We consider the verification of all tumors an absolute necessity. To be conspicuously noted in the appraisal of treatment of any kind for tumors of this type was the natural long life of many of the patients with minimal treatment.

The transcranial surgical approach is, in our opinion, the most favorable approach. It provides better visualization and direct surgical verification, the opportunity for complete removal of localized lesions, with ultimate cure, and the chance of lessened cosmetic defect postoperatively. Enucleation of the eye or exenteration of the orbit seems unwarranted. Follow-up studies on patients treated by surgical measures alone, or by operation followed by irradiation, are included. The role of x-ray therapy alone for tumors of the optic nerve is not evaluated.

Section of Neurologic Surgery.

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Intracranial Arteriovenous Aneurysms

A Study of Their Effect on the Cardiovascular System

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Arteriovenous aneurysms in the arteries of the extremities may cause large arteriovenous shunts, increasing the minute volume of the heart and thereby its work. If such a shunt is permitted to continue long, it may cause cardiac insufficiency (high output failure). Experimental arteriovenous aneurysm has been used to induce cardiac insufficiency. Many separate observations on patients with intracranial arteriovenous aneurysms and cardiac symptoms, especially cardiac insufficiency, have been published in which the opinion was expressed that the aneurysm had caused the cardiac symptoms. It is open to discussion, however, whether or not the heart complications one sees in patients with intracranial aneurysms are actually due to overloading of the heart resulting from a large arteriovenous shunt (Schlesinger and Hazen⁴⁴).

In order to study this question in greater detail, 14 cases of arteriovenous aneurysm were subjected to thorough cardiovascular investigation. In addition, the histories of 123 patients with arteriovenous aneurysm and 10 patients with carotid artery-cavernous sinus fistula treated at Serafimerlasarettet between 1934 and 1953 were reviewed, with particular attention to the occurrence of subjective or objective symptoms from the cardiovascular system.

Methods

The cardiovascular study on the 14 patients included tests of heart function, blood volume determinations, roentgen examination of the heart,

and cardiac catheterization. The cardiac function tests were carried out according to the Sjöstrand-Wahlund⁸⁴ method, with pulse and respiration controls and electrocardiograms taken before, during, and after successively increasing exertion in work tests. The work tests were carried out with the cycle ergometer, Holmgren-Mattsson²² model. The working capacity was considered to be that work which was performed in a steady state with a pulse rate of 170 beats per minute and the respiration not exceeding 32 respirations per minute (Wahlund⁸⁴).

It is difficult to give any absolute limits of normal variation in working capacity, but, according to experience gained in institutions where the above method is used, it is believed that women should be able to tolerate a load of at least 600 kg. per minute and men a load of at least 900 kg. per minute. Comparable values were also obtained in the City of Stockholm health examinations in 1954 (Frisk, Werkö, Holmgren, and Ström¹⁵). According to Kjellberg, Rudhe, and Sjöstrand,²⁰ there exists a close correlation of the heart volume, blood volume, and physical-exercise tolerance. The ranges of normal variation for these data have been set up by Holmgren et al.,²² and these figures have been used in the present study. Holmgren and associates give the heart volume with the patient in the prone position, whereas in our material the roentgen examinations of the heart were done with the patients in the standing or sitting position (Jonsell²⁰). This difference in technique may cause certain deviations primarily a decrease in the heart size in orthostatic reaction. When there has been reason to suspect this, the examinations have been supplemented with roentgenograms taken with the patient in the prone position. The size of the heart is reported both as an absolute value and in milliliters per square meter of body surface area. The normal value was considered to be 900 ml., or 450 ml/sq. meter BSA as the upper limit (Jonsell, Lysholm, Nylin, and Quarnä; cf. Jonsell²⁰). Determinations of the total hemoglobin and blood volume were made according to Sjöstrand's alveolar carbon-monoxide method (Sjöstrand⁴⁶). The normal values for total hemoglobin are approximately 1% of the body weight in men

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INTRACRANIAL ARTERIOVENOUS ANEURYSMS

TABLE 1.—Clinical Data in Fourteen Cases of Arteriovenous Aneurysm

Case No.	Sex	Age, Yr.	Length of History, Yr.	Symptoms and Signs	Localization	Size, Mm.	Determination of Physical Working Capacity	Heart Catheterization
1	F	38	28	Between 10 and 24 yr. age about 8 subarachnoid bleedings; no focal neurologic signs	Right parietal	35×40×40	+	—
2	M	16	8	At 8 yr. age subarachnoid + intracerebral bleeding; death after 14 yr.; hemiplegia	Brain stem	30×30×35	—	+
3	F	40	30	Since 10 yr. age attacks of dizziness; since 20 yr. attacks of weakness of left arm and leg; since 35, Jacksonian epilepsy	Right parietal	35×55×35	+	—
4	M	37	17	At 20 yr. age intracerebral bleeding; hemiplegia	Left Sylvian fossa	40×50×50	+	+
5	M	35	5	At 30 and 35 yr. age subarachnoid bleeding; no focal signs	One suprasellar; One in region of r. caudate n.	30×30×35 10×10×10	+	+
6	M	54	23	At 31 yr. age subarachnoid and at 40 yr. intracerebral bleeding; hemiplegia	Left parietal (new angiogram 2 yr. later: no evidence of aneurysm)		+	+
7	F	63	28	Epilepsy; no focal signs	Left temporal	35×35×35	+	+
8	M	47	27	Headache; swelling of left temporal region	Extracranial	13×30×10	+	+
9	M	48	3	Epilepsy; no focal signs	Right parieto-occipital	45×70×50	+	+
10	M	34	7	Jacksonian epilepsy; slight weakness of right arm	Left parietal	35×40×35	+	+
11	F	39	4	Diminished vision last 4 yr.; right eye 0.6, left eye 1.0; blurred discs bilat.	Right frontal	50×30×30	+	+
12	F	40	14	Epilepsy; no focal signs	Left fronto-temporal	35×35×40	+	—
13	M	51	10	Since 41 yr. age slowly increasing weakness and numbness in right half of body	Posterior cerebral fossa, left side	30×30×20	+	—
14	M	36	17	At 19 yr. age subarachnoid bleeding; last few months epilepsy; no focal signs	Left Sylvian fossa	20×25×65	+	—

and somewhat less in women. The values for blood volume obtained with Sjöstrand's method agree closely with the blood volume determinations with Evans blue and radioactive phosphorus (P^{32}) (Wiklander⁶⁸).

Cardiac catheterization was performed according to the method described by Courmand,⁸ with later modifications. The cardiac output was determined according to Fick's principle, with analysis of the oxygen in the blood from the pulmonary and brachial arteries according to Van Slyke and in expired air according to Haldane. The blood pressure in the systemic and in the pulmonary circulation was measured with Elema strain-gauge manometers. The technique has been discussed in detail by Eliasch.¹¹ Concurrently, the renal inulin and para-aminohippurate clearances were determined (Smith⁶⁹).

It is evident from the data presented in Table 1 that all these methods were used in the majority of cases. In some cases in which the patients had had subarachnoid hemorrhage in the weeks immediately preceding the investigation, however, cardiac catheterization and cycle ergometry were not done. In one case the cardiac catheterization had to be interrupted because the patient became too anxious and nervous.

Material

Altogether, 14 patients were examined, 9 men and 5 women. The ages ranged from 16 to 63

years, with an average age of 41 years. The mean duration of the clinical symptoms was 16 years. The aneurysms were relatively large in all cases, varying in size from that of a walnut to that of a tangerine.

The principal symptoms, as well as the site and size of the aneurysms, are given in Table 1.

In addition to the foregoing series, the histories in 123 cases of arteriovenous aneurysm and 10 cases of carotid artery-cavernous sinus fistula treated at Serafimerlasarettet between 1934 and 1953 were studied, with particular attention to cardiovascular symptoms. Both electrocardiograms and heart roentgenograms had been made in 4 cases, only electrocardiograms in 28 cases, and only heart roentgenograms in 3 cases.

Results

In the 14 cases subjected to thorough cardiac investigation, the histories showed no important symptoms referable to the cardiovascular system except in 2 (Cases 6 and 9). In Case 6 there was dyspnea following exertion, and the patient had already auricular fibrillation at rest. In Case 9 there were mild symptoms of angina-pectoris type following exertion,

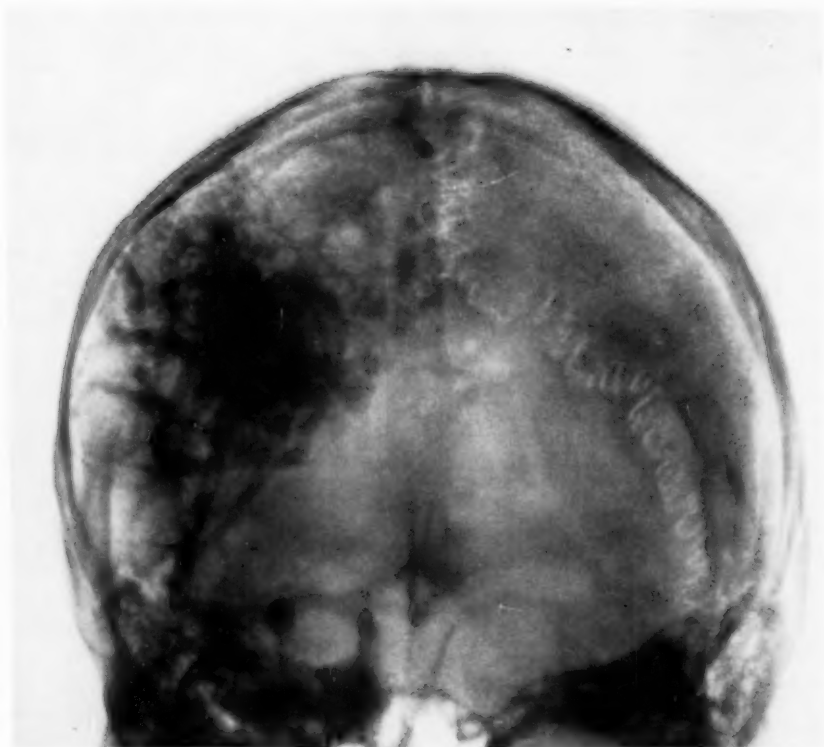


Figure 1A

Fig. 1. (Case 9, Table 1).—Arteriovenous aneurysm in the right parieto-occipital region.

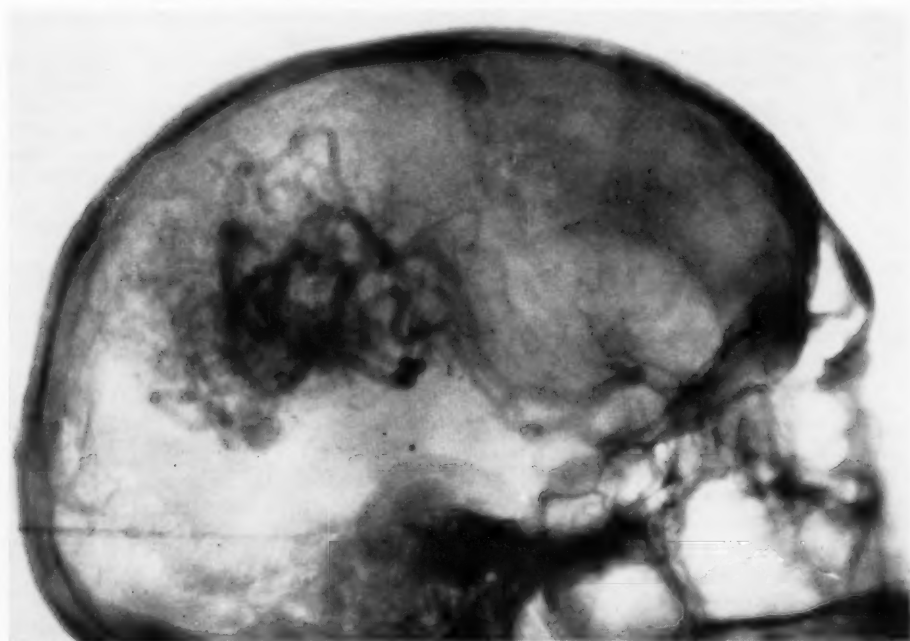


Figure 1B

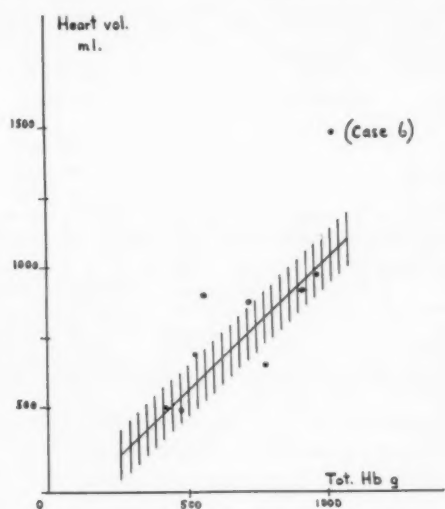


Figure 2

Fig. 2.—Correlation of heart volume with total hemoglobin. The hatched area indicates the

without, however, definite signs of coronary insufficiency during work tests.

Cycle ergometry tests of cardiac function were carried out on 12 of the 14 patients. Two of these patients (Cases 4 and 6) had considerable hemiplegia, which presented certain difficulties in the performance of the test. The physical-exercise tolerance was comparatively ordinary. Roentgen examination showed definite heart enlargement in Case 6, as expressed by both absolute and relative values. In one patient (Case 14) the size of the heart could not be definitely determined because of old tuberculous changes in the lungs. Electrocardiograms made during rest were normal in all cases, except in Case 6, and no definite pathologic electrocardiographic changes were registered during or after exertion. The exercise tolerance test did not have to be interrupted in any case because of cardiac symptoms.

Figures 2, 3, and 4 show the correlation between the heart volume and the total hemoglobin, between heart volume and working capacity, and between working capacity and total hemoglobin. It may be seen that the values fell definitely outside

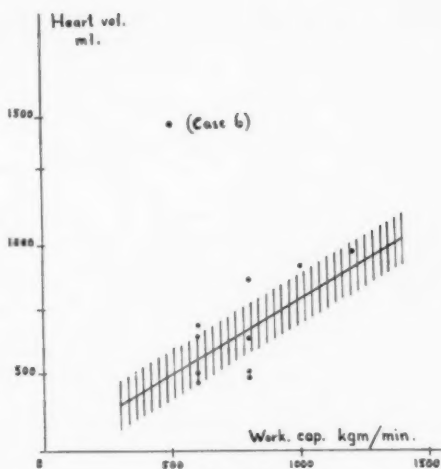


Figure 3

normal variations. Only case 6 falls pathologically beyond normal limits.

Fig. 3.—Correlation of heart volume and working capacity.

the normal range of variation given by Holmgren et al.²³ in only one case (Case 6).

Table 2 shows values for the arteriovenous oxygen difference, the cardiac output, and the blood pressure in the systemic and pulmonary circulations. For comparison, we have set up corresponding values for a

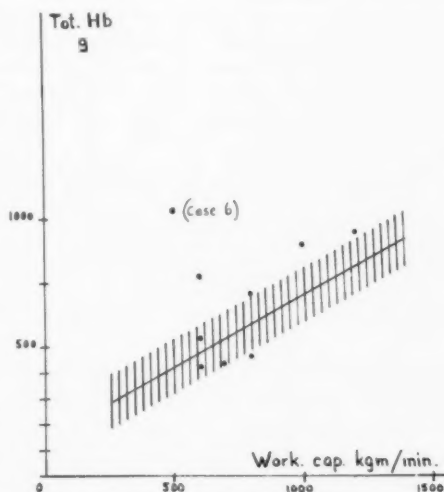


Fig. 4.—Correlation of heart volume and total hemoglobin.

TABLE 2.—Cardiac Output and Blood Pressures in Systemic and Pulmonary Circulation in Eight Patients with Intracranial and One Patient with Extracranial Arteriovenous Aneurysm*

Case No.	Age, Yr.	Cardiac Index, L/Min/Sq. M. BSA	Pulse Rate, Beat/Min.	A-V O ₂ Diff., Ml/L.	Blood Pressure, Mm. Hg							
					PCV	RA	PA			BA		
							S	D	M	S	D	M
2	16	4.70	81	27	--	4	18	8	13	132	71	88
4	37	3.13	71	34	--	0	12	4	8	119	69	87
5	35	3.33	83	42	8	3	29	11	18	122	68	88
6	54	2.31	82	58	6	1	20	10	14	124	81	90
7	63	2.78	69	42	--	2	--	--	--	129	55	90
8	47	3.91	81	36	--	1	23	4	11	139	81	103
9	48	2.77	80	39	--	3	20	9	13	139	77	98
10	34	4.67	71	30	9	1	22	8	13	125	69	87
11	38	3.34	83	33	--	4	15	7	10	110	65	92

* BSA=body surface area; A-V O₂ diff., arteriovenous oxygen difference (between brachial and pulmonary arterial blood); PCV, pulmonary capillary venous; RA, right atrium; PA, pulmonary artery; BA, brachial artery; S, systolic; D, diastolic; M, mean.

normal material and for a series of 11 cases of patent ductus arteriosus, which may be said to be a form of arteriovenous anastomosis (Table 3). In cases of intracranial aneurysm the cardiac output is normal—in a number of cases almost low—and shows no correlation with the size of the aneurysm. The blood pressure—even the pulse pressure in the arterial system—is normal in all cases.

Table 4 shows the renal clearance tests. The values are all completely within the normal limits, indicating that the circulation is not under stress.

In one case showing relatively high cardiac output, blood was taken from the subclavian vein on both sides at the opening of the left jugular vein. On the side where the aneurysm was situated, the oxygen saturation was 0.3 vol.% higher than on the other side. This difference lies well within

the margin of error of the method. Therefore, it is unlikely any larger quantity of blood passed through the aneurysm.

A review of the histories in 123 cases of arteriovenous aneurysm and 10 cases of carotid artery-cavernous sinus fistula gave the following information:

Hypertension.—This was present in five cases. In these cases the systolic blood pressure was 170 mm. Hg or higher and/or the diastolic was 100 mm. Hg or more. The blood pressure was controlled in some cases on several occasions. This is especially true of patients who were admitted with a relatively fresh intracranial hemorrhage and with initially somewhat raised blood pressure. In these cases we report here only the blood pressure registered when the pa-

TABLE 4.—Para-Aminohippurate (PAH), Creatinine, and Inulin Clearances* in Eight Patients with Intracranial and one Patient with Extracranial Arteriovenous Aneurysms

TABLE 3.—Cardiac Index, Arteriovenous Oxygen Difference, and Pulmonary Arterial Mean Pressure in Present Material (A, av.) Compared with Values in a Material of Patients with Patent Ductus Arteriosus (PDA) and of Healthy Subjects (N)

		No.	Mean	S. E. *	S. D. *
Cardiac index, L./min./sq. m. BSA (pulm.)	A av	9	3.44	±0.882	±2.646
	N	18	3.56	±0.149	±0.634
	PDA	11	4.97	±0.68	±2.27
A-V O ₂ diff., ml/L.	A av	9	37.9	±3.03	±9.10
	N	18	38.3	±1.64	±9.96
Pulmonary arterial, mean pressure, mm.	A av	9	12.5	±1.05	±2.98
	N	18	9.7	±0.41	±1.75

* S. E. indicates standard error; S. D., standard deviation.

Case No.	Clearance, ml/Min/1.73		
	PAH	End. Creat. †	Inulin
2	570	77	129
4	641	89	117
5	559	87	110
6	418	93	126
7	451	83	82
8	516	95	103
9	573	136	164
10	710	128	176
11	505	92	94
Mean	549.3	97.8	122.3
Normal mean	569.6		
PDA ‡ mean	483.8	90.4	120.1

* The mean values are close to the normal values. The renal blood flow (PAH clearance) is higher than in a comparable material of patients with patent ductus arteriosus.

† End. creat.=endogenous creatinine.

‡ PDA=patent ductus arteriosus.

tient was in a clinically less disturbed condition.

CASE A. av. 35.—A woman aged 29 had, 10 months before admission, sustained a traumatic carotid artery-cavernous sinus fistula, with considerable unilateral exophthalmos. Examination of the heart showed the second pulmonary and second aortic tones to be accentuated. There was a weak systolic murmur over the whole heart. The blood pressure was 210/130. The patient had no subjective cardiac symptoms. She underwent operation, with ligation of the internal carotid artery in the neck and intracranially. This was done in two sessions. Thereafter the murmur disappeared, and the exophthalmos regressed almost completely. The patient died 12 years after discharge from the hospital in cerebral hemorrhage. During the last years she had had increasing hypertension (250 mm. Hg systolic) and moderate decompensation symptoms.

CASE A. av. 120.—A woman aged 50 was admitted with a two-year history of timitus and slight visual impairment. Angiographic examination showed an aneurysm in the occipital region. Her blood pressure was 170/120. The aortic second tone was accentuated, and an electrocardiogram showed a right bundle-branch block.

CASE A. av. 126.—A man aged 47 had a history of Jacksonian epilepsy since the age of 40. He had had nephritis for the last 10 to 15 years. His pulse had been irregular the last five years. Angiograms showed an arteriovenous aneurysm, the size of an orange, in the parietal region. Examination revealed no heart murmur and no other cardiac abnormality. His blood pressure was 180/130. Electrocardiograms showed auricular fibrillation plus ST-T changes over the left ventricle of left-ventricular-strain type.

CASE A. av. 148.—A 68-year-old woman had a several years' history of high blood pressure, exceeding 200 systolic the last year, with epilepsy the past two years. Examination of the retinas showed second-degree hypertensive changes in the fundi. Angiography revealed an arteriovenous aneurysm half the size of a tangerine. This patient died in cerebral hemorrhage one year after discharge. Autopsy showed moderate coronary sclerosis.

CASE A. av. 151.—A woman aged 61 had a 20-year history of Jacksonian attacks. For the last several years she had exhibited mental changes, in the form of loss of memory and difficulty in concentrating, as well as dyspnea and heart palpitation. Her blood pressure was 200/120. Electrocardiography showed sinus tachycardia.

Electrocardiographic Changes.—Pathologic electrocardiographic changes occurred

in three cases, without other accompanying symptoms.

CASE A. av. 138.—A man aged 22 had acute subarachnoid hemorrhage together with a slight intracerebral hemorrhage one month before admission. His aneurysm was located in the right temporal lobe adjacent to a hemorrhagic cavity. Electrocardiographic examination 40 days after the hemorrhage showed signs indicating coronary insufficiency with myocardial involvement in the area of the left ventricle. Electrocardiograms made on the 50th and 51st days after the hemorrhage showed nothing definitely pathologic. Roentgen examination of the heart showed 750 cc. volume, corresponding to 420 cc. per square meter of body surface.

CASE A. av. 152.—A woman aged 34 sustained subarachnoid hemorrhage. The arteriovenous aneurysm was situated in the left temporal lobe. Electrocardiograms made 18 days after the hemorrhage (her condition was still somewhat affected) presented generally low peaks—"diffuse myocardial effect." Follow-up examination in 1955, i. e., two years after discharge, showed nothing pathologic.

CASE A. av. 115.—A man aged 22 after one year's history of headache attacks, had subarachnoid and intracerebral hemorrhage. The site of the arteriovenous aneurysm was in the left temporal lobe. Electrocardiograms a few days after the hemorrhage showed bigeminy and a negative T₁-wave.

Subjective Heart Symptoms.—The histories showed such symptoms in only one case.

CASE A. av. 87.—A woman aged 52 had had diphtheria at the age of 20. For several years before admission she complained of shortness of breath and palpitation of the heart. Examination revealed no objective physical signs relative to the heart. No further examination of the heart was done. The arteriovenous aneurysm in the occipital region was extirpated. Follow-up by letter seven years later showed the patient to be fully capable of working.

Objective Decompensation Symptoms.—These were not demonstrated in any of the cases.

Comment

Earlier Investigations.—Man's brain weighs about 1400 gm. and represents only 2% of the weight of the entire body, but it receives about one-sixth of the blood pumped out from the heart and accounts for 20% of the oxygen requirement of the

entire body. It is believed that one unit of brain tissue receives 25 times as much blood as a corresponding unit of resting skeletal muscle (Gerard¹⁶).

Studies on the circulation in the brain with Kety and Schmidt's²⁸ technique have shown the normal value in young men at rest to be 54 to 65 cc. of blood per 100 gm. of brain per minute, or about 750 cc. per minute through the whole brain. The normal range of variation is said to be between 500 and 1000 cc. (Kety²⁹; Himwich¹⁹). The highest values observed have been in cases of intracranial arteriovenous aneurysm (A. av.), where various writers report finding values in certain cases as high as 200 cc. per 100 gm. of brain tissue per minute (Shenkin et al.⁴⁵; Bodechtel⁵; Tönnis,⁵³ *inter alios*). Accordingly, in this pathologic condition about 2800 cc. per minute would pass through the brain, as opposed to the normal 750 cc. These investigations would seem, therefore, to indicate that the heart is subjected to a greater load when these shunting mechanisms are coupled into the blood stream.

Knowledge on how the cardiovascular system reacts in cases of arteriovenous aneurysm is based principally on the behavior in traumatic arteriovenous aneurysms in the extremities. It has long been known, of course, through studies by Holman,^{20,21} Rienhoff,⁴¹ Reid,³⁹ McGuire,³³ McGuire et al.,³⁴ and Pendergrass,³⁸ *inter alios*, that if the aneurysm attains a certain size it may affect the entire cardiovascular system, with dilation of afferent and efferent vessels and enlargement and hypertrophy of the heart. Reid is of the opinion that the acquired aneurysms differ from the congenital form in that the latter does not affect the cardiovascular system at all.

Observations have been made supporting the contention that intracranial arteriovenous aneurysms can affect the cardiovascular system, resulting in notable clinical symptoms. In this connection, Steinheil⁵⁰ (1895) described a case in which enlargement of the heart was present, and was

even confirmed at autopsy (slight hypertrophy of the right ventricle). Emanuel¹⁴ (1899) discussed a case of arteriovenous aneurysm in a 36-year-old man who had presented signs of enlargement of the heart even in childhood. Autopsy showed cardiac hypertrophy. In this case both vertebral arteries were appreciably dilated as well. Isenschmid²⁵ (1912) described clinical signs of cardiac enlargement in a 9½-year-old girl with an arteriovenous aneurysm located both intracranially and extracranially. Roentgenograms showed diffuse enlargement of the arch and the ascending portion of the aorta. Ligation of the carotid artery was done. The vascular murmur on the calvaria (calotte) decreased subsequently, only to regain the same magnitude after several days. The girl died 13 years later, and the results of autopsy were reported by Herzog¹⁸ (1927) briefly as follows: "*Keine ausgesprochene Veränderungen am Herzen und peripheren Gefäßapparat.*" Eimer and Mehlhose¹⁰ (1927) also observed a moderately dilated heart in a 23-year-old woman. This was confirmed by roentgen examination. Brock and Dyke⁷ (1932) found the heart somewhat enlarged in four of five cases. Röttgen⁴² (1937) was of the opinion that he had demonstrated in one of his four published cases of arteriovenous aneurysm that cardiac enlargement had been present and had disappeared two months after ligation of the carotid artery. However, it is impossible in this case to draw any definite conclusions concerning the cardiac enlargement with subsequent normalization, as no data on heart volume determinations are given. This criticism applies also to the work of earlier cited writers with respect to roentgen examination, inasmuch as the examining technique was still undeveloped at that time. Comparison of the heart roentgenograms published by Röttgen shows also that the thorax is in the position of increased inspiration in the view showing the decrease in the size of the heart postoperatively. Moreover, the reduction in the heart volume

that may be a direct result of the confinement to bed in conjunction with the operation does not seem to have been taken into consideration (Karnell²⁷). This question again became one of current interest when Shenkin et al.⁴⁵ (1948) reported two cases of arteriovenous aneurysm in which the cerebral blood flow also was studied with Kety-Schmidt's technique. In both cases there were cardiac enlargement and increased cardiac output, determined with ballistocardiography. Bodechtel⁵ (1952) described two cases in which exertion caused dyspnea and cyanosis. These symptoms disappeared after extirpation of the aneurysm. Bernsmeier and Siemons³ (1952) also reported two cases out of six in which there were symptoms of cardiac decompensation. In all six cases clinical signs of cardiac enlargement were observed. In a review of 72 cases of arteriovenous aneurysm, Tönnis and Lange-Cosack⁵³ (1953) state, more or less *en passant*, that in some cases signs of cardiac enlargement, as well as differences in pulse and blood pressure, were present. Matson³² (1954) mentioned that he had seen two infants who died in cardiac failure within the first week of life. Each was found at necropsy to have "virtually one-half of the hemi-cranium replaced by a massive cortical arteriovenous malformation." Ask-Upmark¹ (1955) presented a brief description of a patient with an extracranial arteriovenous aneurysm who died at the age of 64 in cardiac decompensation. In a review of 100 cases, Paterson and McKissock³⁷ found that 9 showed raised pulse pressures and clinical or radiologic evidence of enlargement of the heart to the left. In one instance cardiac catheterization revealed an abnormally high oxygen content of the venous blood entering the heart. Detailed data on these two cases are not given. Streeter,⁵¹ in his classic study on the embryonal vascular development in the brain, states that the arteriovenous aneurysm may conceivably arise in conjunction with the splitting of the vascular system of the head into three superimposed layers by the

development of the skull, the dura, and the pia, and that at this stage embryonic arrest of a portion of the vascular system of the head takes place. In this way pathologic vascular connections may persist. It might perhaps be expected that a disturbance in the embryonal vascular development in the brain would be reflected in a disturbance of the vascular development in the viscera. Evidence of such an association has been presented by Broager and Hertz,⁶ who found 4 cases of intracranial arteriovenous aneurysms among 200 patients with congenital heart failure.

Thus, there is support for the contention that in certain cases arteriovenous aneurysms may be combined with clinical symptoms referable to the cardiovascular system. However, the clinical observations cited are sporadic, and in some cases lack sufficiently detailed investigation to permit their acceptance as definite proof without further ado. In the monograph by Bergstrand, Olivecrona, and Tönnis,² and in the report by Olivecrona and Riives³⁶ on 43 arteriovenous aneurysms, it would seem that the effect on the cardiovascular system in the case of the arteriovenous aneurysm is of no significance. In Sattler's⁴³ extensive study, with analysis of 214 traumatic and 71 spontaneous arteriovenous fistulas between the internal carotid artery and the cavernous sinus, no comment is made on whether or not the fistulas had a damaging effect on the cardiovascular system. Dandy⁹ stated he had not observed any symptoms from the cardiovascular system in his thorough investigation of eight cases of fistula between the internal carotid artery and the cavernous sinus. Schlesinger⁴⁴ had the same experience in a study based on 37 cases of aneurysm: "In no case was there any striking evidence of serious cardiovascular abnormality which might be interpreted as secondary to the cerebral fistula, such as occurred in Shenkin's two cases."

Our Investigation.—The greatest care, of course, must be observed in evaluation of questions in this field on the basis of case

histories alone. Minor cardiac symptoms may have escaped the examining physician. All that could definitely be established through a study of the case histories was that in only one case (A. av. 87) were there cardiac symptoms which led to special notation. In five cases there were also signs of hypertensive cardiovascular disease of sufficient severity that that pathologic condition in itself could have caused cardiac insufficiency, a possibility which, as is evident from the foregoing review of the literature, has seldom been precluded. Of course, the arteriovenous communication has nothing to do with the origin of the hypertension. With respect to the cases in which only electrocardiographic changes were observed, it should be pointed out that in subarachnoid hemorrhage transient electrocardiographic changes of central origin are usually observed initially. A pathologic electrocardiogram immediately after a hemorrhage is not a definite indication of cardiac disease. As demonstrated by some of our cases also the electrocardiographic changes may later disappear. We should like to note here that in the series of 14 cases subjected to thorough cardiac investigation we made an effort to select patients who had had symptoms over a long period, and so an eventual cardiovascular change would have had time to develop. The arteriovenous aneurysm usually increases somewhat in size with the passage of time (Höök and Johanson²⁴).

One patient (Case 6) had slight enlargement of the heart on roentgenograms and decreased working capacity. These observations might be interpreted as signs of overloading due to a large shunt. As the cardiac output was low in this case, the cardiac enlargement could not have been caused by the arteriovenous shunt, but, rather, was a sign of incipient heart failure of other origin. This is indicated also by the presence of auricular fibrillation. It was found later in new angiograms, taken 21 years after the first, that the aneurysm had become thrombosed. This case, with respect to the roentgen findings, has been discussed by Höök

and Johanson.²⁴ It illustrates the necessity of carrying out a thorough cardiovascular study before the intracranial shunt may be considered in any way to constitute a cause of cardiovascular disease.

Conclusion

Our physiologic studies provided no basis for assuming that intracranial arteriovenous aneurysms had resulted in shunts of an order to overload the cardiovascular system. In our material of intracranial arteriovenous aneurysms, all values for cardiac output, pressure in the pulmonary circulation, and renal clearance tests lay within normal limits. Our study should be viewed against the background of the investigation carried out in 1951 by Warren, Nickerson, and Elkin⁵⁵ on an extensive material of traumatic arteriovenous aneurysms, located principally in the extremities, and always outside the skull. In this material the cardiac index proved always to be high. In cases of aneurysm in the femoral and iliac region the cardiac index was between 6.0 and 7.1 per minute per square meter of body surface. It was lower in cases of aneurysm in the subclavian, carotid, and vertebral arteries (4.0 to 4.5 per minute per square meter BSA), and in our material it varied between 2.3 and 4.7 per minute per square meter BSA. Thus, in their material of extracranial aneurysms there was also a tendency to smaller shunts in aneurysms near the cranium.

Summary

Thirteen cases of intracranial and one of extracranial arteriovenous aneurysm were investigated with consideration directed to the heart and circulation. In no case were there symptoms indicating an increased load on the heart and circulation resulting from the arteriovenous aneurysm.

The histories of 123 cases of intracranial arteriovenous aneurysm and of 10 cases of carotid artery-cavernous sinus fistula were studied with consideration given to the cardiovascular symptoms. Neither was it possible in this material to demonstrate

symptoms indicating an increased load on the heart and circulation that could be regarded as caused by the arteriovenous aneurysm.

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Clinical Correlates of Electroshock Therapy

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Advances in psychiatry have paralleled rather closely the advances achieved in other branches of medicine. The initial descriptive phase gave recognition to the principal clinical entities to be dealt with in the field. This was accompanied and followed by a period concerned with psychodynamics and the relation of man to his environment. More recently, however, physiologic and biochemical advances have given a new impetus to psychiatry, in common with almost every other branch of medicine. Shock therapies have achieved dramatic results, and further experience has indicated the potentialities and limitations of these measures. Psychosurgery has also produced beneficial therapeutic effects and has proved to be a valuable tool in exploring the relation of neurophysiology to psychiatry. Still more recently a new field that may properly be designated as psychopharmacology has emerged and is advancing rapidly as the effects of various pharmacologic and endocrine preparations on psychiatric conditions are determined.

The majority of the recent advances referred to in the field of experimental psychiatry have been made empirically, and the basis of their effect, or mode of action, has not been determined.¹ Previous reports^{2,3} have reviewed, for example, the many investigations which have been conducted to explain the beneficial clinical effects of electroshock therapy and indicated their uniformly negative results. Numerous hypotheses have been elaborated to bridge this disappointing void,^{1,4} but have involved neurophysiologic mechanisms, which (from

what is known of such processes) are difficult to correlate with the relatively prolonged clinical effects of electroshock therapy. In view of the results obtained in our own studies,^{2,3} which have shown that the permeability of the blood-brain barrier is markedly increased following a series of electrically induced convulsions and that this basic neurophysiologic mechanism is capable of conditioning cerebral neurophysiology over somewhat prolonged periods, a possible explanation of electroshock therapy is suggested, which deserves further consideration. It is the purpose of the present paper to discuss the theoretical implication of these studies and to place them in proper perspective with respect to clinical and other related neurophysiologic data. A review of the studies referred to, however, is essential before their significance can be discussed to advantage.

Effect of Electrically Induced Convulsions on Permeability of Blood-Brain Barrier

Studies which have utilized a modified spectrochemical technique for following the distribution of cocaine used as a tracer agent have been performed on cats under control conditions and after a series of electrically induced convulsions, in accordance with methods fully described in an earlier publication.² Specifically, the object of these experiments was to determine whether or not alterations in the concentration of cocaine occurred in the central nervous system after a series of electrically induced convulsions, which might reflect permeability effects in the blood-brain barrier of possible neurophysiologic significance in explanation of the clinical results obtained with electroshock therapy.

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Similar studies, following preliminary injections of trypan red, were made,³ inasmuch as this supravital dye had been shown in previous investigations^{5,6} (1) to stain uniquely the endothelial cells of the cerebrovascular tree without itself gaining entrance into the nerve tissue proper; (2) to lower the permeability of the blood-brain barrier and to prevent abnormal increases in the permeability of this barrier, such as occur in many abnormal conditions of the central nervous system, and (3) to counteract the cerebral dysrhythmia usually produced in experimental cerebral concussion, as well as the increased permeability observed with concussion,⁶ a finding which suggested that the dysrhythmia was neurophysiologically related to and dependent upon the altered blood-brain-barrier effect. These findings had suggested that the blood-brain barrier is a basic neurophysiologic mechanism capable of conditioning the neurophysiology of the central nervous system over relatively prolonged periods.⁷ Since the permeability of the blood-brain barrier had been markedly increased in our initial study on electroshock, it seemed pertinent to repeat the same experiments after injection of trypan red in order to determine whether this agent might counteract the permeability and cerebral dysrhythmic effects of electrically induced convulsions, as had been found after cerebral concussion.⁶ The determination of this point also appeared crucial if the increased permeability of the blood-brain barrier* is to be related directly to cerebrovascular permeability, as postulated by Spatz.⁸

The use of trypan red also suggested interesting possibilities with respect to the question of current pathway in electroshock therapy. There is reason to believe on

neuropathologic and physiologic grounds that a high percentage of the current traversing the brain in electroshock therapy is transmitted along the vascular tree of the brain or in its blood stream.³ Neuropathologic studies following excessive electroshock currents,⁹ for example, have shown vascular and perivascular changes in the main, and thus would be consistent with this concept. If this is correct, the physiologic effect of electroshock might be presumed to be confined primarily to the cerebrovascular tree, and trypan red, which uniquely stains the endothelium, might be used to test this point. If, on the other hand, the transmission of electric current is primarily mediated through cerebral nerve tissue per se, as has been postulated by several investigators,¹⁰⁻¹⁴ and if the effects of electroshock are of neurogenic origin, rather than cerebrovascular, it would seem unlikely that trypan red would abolish the cerebral dysrhythmia associated with a series of electrically induced convulsions.

Correspondingly, a series of electrically induced convulsions were produced in cats, and studies were conducted in a fashion identical with the initial study in all respects, except that the cats received preliminary injections of trypan red.³

Methods.—Adult cats were selected on the basis of their showing a normal electroencephalogram. Four series of experiments were performed, with determinations of the concentration of cocaine in the blood and brain of the cats under the following conditions: (1) a control study, without pretreatment with trypan red and without electroshock treatment; (2) without pretreatment with trypan red but with electroshock treatment; (3) with the pretreatment of trypan red but without electroshock treatment, and (4) with pretreatment by trypan red and with electroshock treatment.

Electroshock treatment was administered in a series of 12 electric shocks given over a period of 22 days, with the usual bitemporal placement of electrodes and with the use of an Offner electroshock apparatus delivering a current of 400 ma. for 0.2 second.

Follow-up electroencephalograms were obtained on all cats after the 7th electrically induced convulsion and, again, three days after the 12th, and final, shock, with the use of a Grass electroencephalographic apparatus.

* In a previous study,⁵ it was pointed out that the term "blood-brain barrier" is confusing and that, if the name is to be retained, it should be restricted to the barrier between the blood and the extracellular fluid of the brain. The presence of another barrier beyond the cerebrovascular tree, and probably located in the cell membranes of the cerebral tissue, was stressed.

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Summary of Statistical Analysis of Data on Distribution of Cocaine Hydrochloride* in Blood and Brain of Cats Under Control Conditions and After Pretreatment with Trypan Red,† Before and After a Series of Electrically Induced Convulsions

Specimen	Pretreatment Trypan Red †	Shock Therapy	No. of Experiments	Mean Value of Cocaine, V./Gm.	Standard Deviation	Signif. Test	Odds ‡
Blood	None	Control (no electric shock)	15	6.2	0.5	0.7	1:1
		After electric shock	14	6.5	0.3		
	Trypan red	No electric shock	9	6.1	0.5	0.0	0.1
		After electric shock	12	6.2	0.5		
Brain	None	Control (no electric shock)	15	28.9	0.9	4.6	2.5×10 ⁻⁴ :1
		After electric shock	14	36.6	1.4		
	Trypan red	No electric shock	10	25.9	1.2	2.0	22:1
		After electric shock	13	22.7	1.0		

* Cocaine hydrochloride, 15 mg. per kilogram of body weight, injected intravenously.

† Trypan red, 1.65 cc. of a 1% solution per kilogram of body weight, injected intraperitoneally. Four such injections were given over a period of from five to seven days.

‡ Odds against results being due to chance.

Four intraperitoneal injections of 1.65 cc. of a 1% solution of trypan red were given over a period of from five to seven days, the dose approximating 10 mg. per kilogram of body weight per injection. A fifth injection of trypan red (same dose) was given between the seventh and the eighth electric shock and 13 or 14 days prior to the final cocaine experiment.

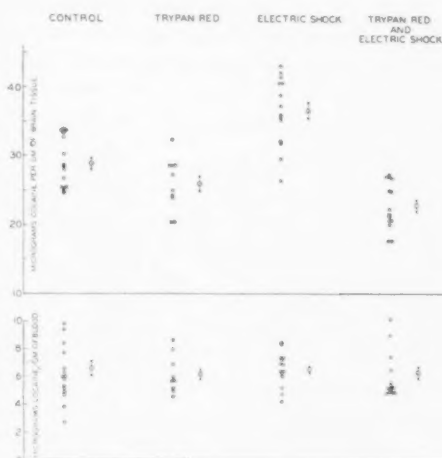
With the cat under moderate narcosis, and in accordance with standardized techniques previously reported,⁹ the final cocaine distribution studies were conducted after the intravenous administration of 15 mg. per kilogram of body weight of a 6% solution of cocaine hydrochloride in both control and postshock cats. In the case of the postshock group the cocaine studies were performed three days after the completion of the electroshock series of treatments. The cocaine was injected slowly and evenly over a 15-minute period. At five-minute intervals thereafter, specimens of brain and blood were obtained and immediately frozen in solid carbon dioxide (carbon dioxide snow). The brain and blood specimens were extracted chemically by standardized methods, which we have previously described,¹⁰ and finally analyzed for cocaine by means of a spectrophotometric technique, utilizing a Beckman photoelectric spectrophotometer.

Results.—The results are presented graphically in the accompanying Figure, and an analysis of the data is shown in the Table.

In the experiments without pretreatment with trypan red, significant and persistent rises in the concentration of cocaine were found in the cerebral cortex after repeated electroshocks which induced convulsions. Since no change was observed in the con-

centration of cocaine in the blood of these same animals after electroshock, it was concluded that a series of electrically induced convulsions increased the permeability of the blood-brain barrier.

In the experiments with trypan red pretreatment, cortical concentrations of cocaine were found in the group given electroshock treatments which were equal to or lower than the corresponding control values



Spot graph showing the spread of experimental determinations, the mean values, and the standard deviations of the means on the distribution of cocaine hydrochloride in the blood and brain of cats under control conditions, after trypan red injection, and three days after a series of electrically induced convulsions, both with and without previous trypan red injections.

(Figure; Table). Again, no alteration of the blood levels of cocaine were observed in these same experiments. Consequently, it was concluded that trypan red effectively counteracted the permeability effect of electrically induced convulsions on the blood-brain barrier.

A cerebral dysrhythmia failed to develop in the trypan red experiments or appeared only in minor degree. Since trypan red counteracted both the permeability and the dysrhythmic effects of electroshock in these experiments, the results and conclusions of the earlier experiments on cerebral concussion were confirmed, namely, that the dysrhythmia and the abnormal neurophysiologic state reflected by the dysrhythmia were conditioned by the increased permeability of the blood-brain barrier. For the reasons mentioned, these results also suggested that the cerebrovascular tree bore the primary brunt of the electroshock current, and that amounts of the current, sufficient to produce residual neurophysiologic changes that might be correlated with the clinical effects of electroshock therapy, probably were not transmitted through the cerebral cellular masses. Certain of the more obvious implications and limitations of this concept were presented in a previous report.³

Comment

Pertinent to the question of whether the permeability effects of electroshock may be related to its clinical effects is the old observation that electroshock therapy with subconvulsive or "petit mal" currents has little therapeutic value. This is true in the majority of cases, even though smaller "total" currents which still produce convulsions are therapeutically effective. Such results, in addition to the known effectiveness of convulsions when produced by other methods (insulin, pentylenetetrazol U. S. P. [Metrazol]), suggest, as indicated previously, that the physiologic effect of the convulsive phenomenon, and not merely the passage of current, is responsible for the beneficial effect of electroshock therapy.

That the physiologic effect of convulsive phenomena responsible for the therapeutic effects of electroshock may lie in cerebrovascular permeability changes, as demonstrated in the studies referred to, is suggested by the following considerations: (a) Cerebrovascular permeability constitutes a basic neurophysiologic mechanism capable of conditioning the neurophysiology of the central nervous system; (b) as demonstrated in the studies mentioned, this mechanism may be modified over relatively prolonged periods by electrically induced convulsions, and hence might produce neurophysiologic effects that could be correlated with the somewhat sustained clinical benefits of electroshock therapy, and (c) although neurophysiologic processes, directly or primarily involving neuronal elements and pathways, could scarcely be expected from what is known of them to produce persistent effects, the mechanism considered has the advantage of offering an explanation for a sustained conditioning of these elements without itself being dependent upon them.

Neuropathologic studies on excessive electroshock, in addition to the Ferraro reference previously quoted,⁹ have been consistent in showing perivascular changes which were predominant in the cortex and which faded off at deeper subcortical levels.¹⁰⁻²⁵ In view of this evidence, it is of interest to conjecture on the possibility that cerebrovascular permeability changes as produced by electroshock therapy predominate in the cortex, where the maximal pathologic changes have been found. It should be pointed out in this connection that the data presented on the effect of electroshock on the permeability of the blood-brain barrier were based primarily on cortical specimens. The dysrhythmic patterns as obtained by electroencephalography would also be consistent with this concept. However, such electroencephalographic evidence would by no means rule out a more deeply situated cerebral dysfunction. If the effect of electroshock is primarily a cortical

one, as proposed, its action would presumably be due to an intensification of cortical inhibition, inasmuch as this would be in keeping with other neurophysiologic data, including evidence^{5,26,27} which suggests that the neurophysiologic effect of increased cerebrovascular permeability is to increase cortical excitability.

It is of interest to consider this concept in the light of recent advances in the field of psychophysiology and psychopharmacology. Neurophysiologic studies have suggested a functional balance of the inhibitory effect of the cerebral cortex, the reticular activating system of the brain stem, with its diffuse projection system to the cortex, and the hypothalamic centers. An imbalance of these closely interrelated systems has been presumed^{1,28-31} to be concomitant with, if not a cause of, mental disease.

Other components of this balanced functional relationship in the central nervous system have also been suggested. Gloor,³² for example, believes that the amygdaloid complex normally functions in such a way as to modulate autonomic, somatic, and behavior mechanisms. Again, rhinencephalic stimulation has been found to produce "inhibitory" symptoms, including apathy and reduction of emotional expression, along with motor inactivity and loss of contact with the environment.³³⁻³⁶

Psychopharmacological studies have been performed, which also may have a bearing on this subject. Thus, in patients with anxiety, where it is assumed that there is an imbalance in the sense of overstimulation of the cortex from a hyperreactive posterior hypothalamus, the therapeutic effectiveness of chlorpromazine, reserpine,³¹ and azacyclonol (Frenquel)³⁷ has been presumed to depend upon their depressive action on the posterior hypothalamus. Although the evidence suggests that chlorpromazine, for example, depresses this center directly, in larger doses it is also thought that this agent stimulates the reticular activating system,^{29,30} the "alerting" action of which has been presumed to increase the inhibitory

effect of the cortex on the posterior hypothalamus.³⁸

However, since lysergic acid diethylamide (LSD-25), which is capable of producing a "model psychosis," has also been shown to cause an "alerting" response,^{29,30} it is apparent that the interrelationships mentioned cannot as yet be explained satisfactorily in terms of our present knowledge. On the other hand, it would appear fair to conclude from the evidence at hand that a pattern of balanced functional relationships does exist within the central nervous system which is capable of influencing or determining mood and behavior and that in this the role of the cerebral cortex would appear to be an inhibitory one.

The concept of cortical conditioning secondary to cerebrovascular permeability changes as postulated does not preclude similar changes following electrically induced convulsions at deeper diencephalic levels, as has been suggested by other studies.^{1,39,40} Such deeper changes might likewise serve to increase the reactivity of the hypothalamus and thus to produce initial viscerosympathetic manifestations, as noted by Gellhorn³⁹ and others.⁴⁰⁻⁴³

A more comprehensive formulation of the neurophysiologic basis of electroshock therapy would thus include both cortical and hypothalamic components contributing to the final results, both being conditioned by persistent cerebrovascular permeability changes. This hypothesis is attractive, in that it offers an explanation for the relatively prolonged action of electroshock and, by failing to implicate a neuronal effect per se, as envisaged in previous theories, avoids the limitations of a primary neurogenic basis for electroshock therapy.

Summary and Conclusions

Previous studies, which showed that the permeability of the blood-brain barrier was markedly increased by a series of electrically induced convulsions and which suggested that this basic neurophysiologic mechanism was capable of conditioning cerebral neuro-

physiology over somewhat prolonged periods, are reviewed in the light of possible correlations with the clinical effects of electroshock therapy.

Inasmuch as certain clinical considerations, which are discussed, suggest that the therapeutic benefits of electroshock therapy are due to some prolonged neurophysiologic effect of repeatedly induced convulsions, it is concluded that the cerebrovascular permeability changes produced by electrically induced convulsions are probably related to the convulsive phenomenon and not merely to the passage of electric currents.

Further evidence is adduced which suggests that the primary action of electrically induced convulsions, at least in terms of their prolonged effect on cerebrovascular permeability, is cortical rather than subcortical in location and that this may act to condition the cortex neurophysiologically so as to heighten its inhibitory action. If, as has been postulated, the therapeutic effectiveness of shock treatment depends upon the modification of behavioral patterns by hypothalamocortical interaction, the cortical effect of increased cerebrovascular permeability offers an attractive hypothesis which would explain the prolonged neurophysiologic effect of electroshock without implication of a primary neurogenic action. A similar effect at deeper, diencephalic levels is not precluded by this concept, and a final comprehensive formulation of the neurophysiologic basis of electroshock is suggested which involves the conditioning of both cortical and deeper components by persistent cerebrovascular permeability changes.

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Retention of Overlearned Visual Habit After Temporal Cortical Ablation in Monkey

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Many of the symptoms reported by Klüver and Bucy¹ in monkeys after bilateral temporal lobectomy concern changes of visually guided behavior. One aspect of these visual anomalies is the failure to retain preoperatively learned visual discriminations.^{2,3} This detrimental effect is localized in the middle and inferior temporal gyri.^{3,4} Attempts to analyze the nature of this defect show that the memory traces of these habits, the animal's general working attitude, and its visual attentiveness are not disturbed.⁵⁻⁷ Furthermore, there is indication that such temporal neocortical ablations have little effect on an overlearned visual discrimination, i. e., when many additional trials of the discrimination are given to the animal after the usual criterion of learning is reached.¹⁵ Recently, clinical studies have reported that in human patients destruction of medial temporal region abolished only recent, but not old, memories.^{8,9} Experimental studies on such a comparable effect as it appears in animals may help to elucidate its underlying neural mechanisms.

The purpose of the present study is to demonstrate that temporal neocortical ablation in monkeys affects only visual discriminations trained to criterion but not those given additional training after criterion is reached. If such results are obtained, further ablations of the other association areas

will be made to uncover what areas besides temporal cortex participate in preserving these overlearned habits.

Methods

Eight immature monkeys (*Macaca mulatta*) were the subjects of this study. Their body weights at the time they were killed ranged from 2.6 to 5.2 kg. They were trained on three visual discriminations: (a) color, a red plaque (positive) vs. a green plaque; (b) vertical black and white striations (positive) vs. horizontal striations; (c) black disk (positive) vs. black diamond. The general procedure, apparatus used, and specifications of the stimuli were similar to those described in earlier reports.^{8,9} A noncorrection method was used. The criterion of learning was 90% correct in a 30-trial daily session.

The eight subjects were divided into three groups: Four monkeys were in experimental Group I (Monkeys 1 to 4); two were in experimental Group II (Monkeys 5 and 6), and two served as normal controls (Monkeys 7 and 8). All the subjects were trained on the color discrimination first, which was used as a preliminary adaptation problem. The two pattern discriminations formed the main experiments. Two of the animals in experimental Group I (Monkeys 1 and 3) learned the discrimination of vertical vs. horizontal striations before the disk vs. diamond problem. The other two animals (Monkeys 2 and 4) learned these two tasks in a reversed order. Additional 500 trials after criterion were given to Monkeys 1 and 2 on the disk vs. diamond problem, and to Monkeys 3 and 4 on the vertical vs. horizontal striations discrimination. These additional trials were given immediately after the criterion of the specific discriminations was reached. Both animals in experimental Group II learned the striations discrimination prior to the disk vs. diamond problem. Additional 1000 trials after criterion were given to Monkey 5 on the latter problem and to Monkey 6 on the former.

The two control animals also learned the striations discrimination before the disk vs. diamond discrimination. Monkey 7 had 500 additional trials on the latter problem and monkey 8, on the

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vertical *vs.* horizontal striations discrimination. Thus each monkey overlearned one, and learned only to criterion the other, of the two pattern discriminations. For experimental Group I and the control animals the overtraining consisted of giving 500 additional trials, and for experimental Group II, 1000 additional trials. Both the sequence of training on these two pattern discriminations and the choice of the specific discrimination to be overtrained were arranged in a balanced order.

After completion of the preoperative training the six monkeys of the two experimental groups were operated upon. Bilateral ablation of the middle and inferior temporal gyri was performed in one stage under pentobarbital anesthesia with aseptic precautions. Postoperative testing started 14 days after surgery. All the six animals recovered uneventfully. The animals were tested on the three discriminations in a sequence similar to the preoperative order of training. If an animal failed to retain a task, it was retrained to criterion. No additional trials beyond criterion were given on any of the problems.

After the tests following temporal ablation were completed, the two monkeys in experimental Group II (Monkeys 5 and 6) were killed and their brains perfused and removed for histological study. Of the four animals in experimental Group I, two were subjected to bilateral prefrontal ablation in one stage (Monkeys 1 and 2). The parietal cortex of both hemispheres was ablated in the other two (Monkeys 3 and 4). Fourteen days were allowed for recovery after this second operation. Then the animals were again tested on the three discriminations. These tasks were again retrained to criterion only.

Following the completion of retesting after the second operation, the four subjects were given a third operation. The parietal cortex was removed bilaterally in Monkeys 1 and 2, and the prefrontal areas, in Monkeys 3 and 4. Retesting began 14 days after this third operation. The three discriminations were given in order, and the subjects were retrained in them for the fourth time to criterion. These four monkeys of experimental Group I were then killed and their brains perfused and removed for histological study.

Two retention tests were given to the control Monkeys 7 and 8, one in the 7th week and the other in the 13th week after the completion of the original learning. The three discriminations were given in the same order as the original training. The control animals were kept in their living quarters during periods between the retention tests and were not subjected to any surgical or other experimental treatments.

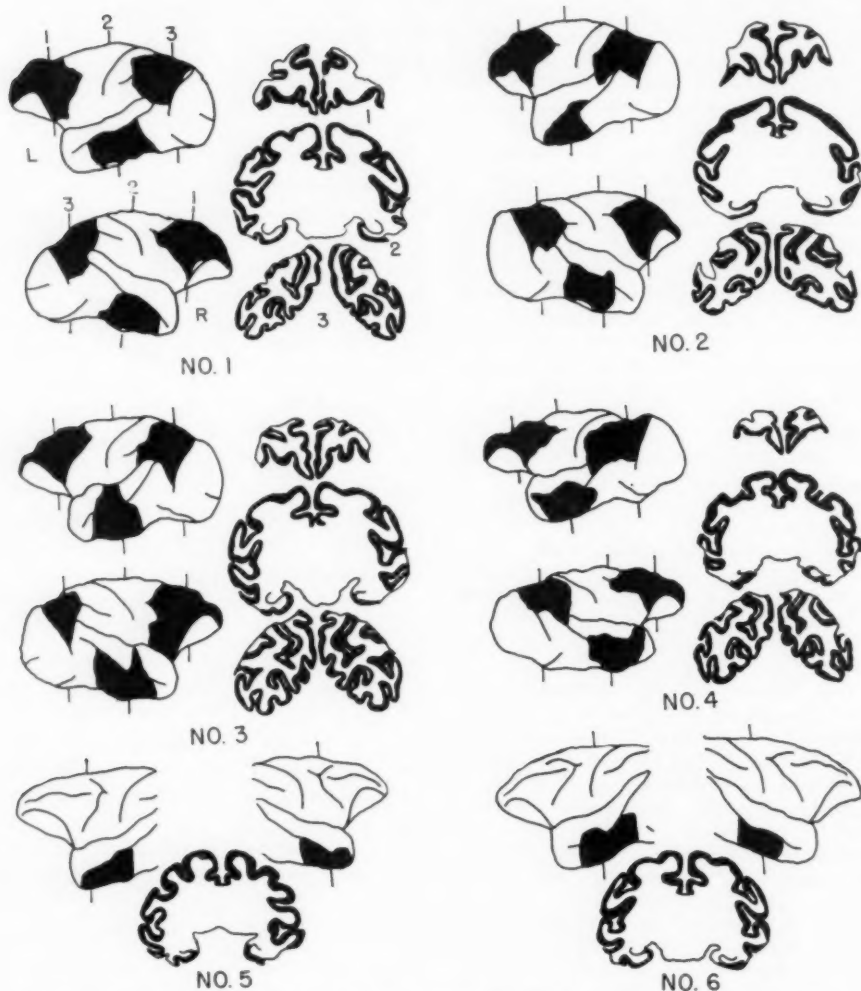
The brains of the six experimental animals were fixed and cut into 50 μ coronal sections, and every 10th section was stained with thionine. The extent

and locations of the cortical lesions were reconstructed and the retrograde degeneration in the thalamus determined.

Results

Anatomical Data.—The Figure gives the reconstruction of the locations and extent of the cortical lesions of all six experimental animals. Representative cross sections through the lesions are also shown. All the temporal neocortical ablations are confined mainly to the middle and inferior temporal gyri. The temporal ablations of Monkeys 3 and 4 are the largest, including a large portion of the superior temporal gyrus. Monkey 6 has a relatively small temporal lesion with the rostral temporal region spared. The frontal extirpations of the four animals in experimental Group I (Monkeys 1 to 4) are all limited posteriorly by the two limbs of the arcuate sulcus and anteriorly to the tip of the frontal pole. The right hemisphere of Monkey 3 shows the only exception; its frontal lesion invades the cortex ventral to the inferior limb of the arcuate sulcus. The parietal lesions of Animals 1 to 4 are all bounded by the lunate sulcus posteriorly. The extent of the lesions in different animals varies in the degree of encroachment upon the postcentral gyrus, anteriorly, and the occipitotemporal region, inferiorly. The left hemisphere of Monkey 4 has the largest parietal removal, and the right hemisphere of Monkey 3, the smallest.

Retrograde degeneration appears in the ventral portion of the nucleus pulvinaris medialis posterior bilaterally in all six experimental animals. This division of the pulvinar nerve sends projection fibers to the temporal cortex.¹⁰ Reflecting the frontal cortical damage, there is severe degeneration in the nucleus medialis dorsalis of the four monkeys in experimental Group I. The degenerated zone as it appears in the cross sections shifts from the lateral two-thirds in the rostral part of nucleus medialis dorsalis to the middle region in its caudal tip. The pattern of degeneration in the present study conforms to the projection plan of



Reconstructions of the location and extent of cortical lesions of the experimental animals. The cortical lesion is indicated by solid black. The positions of the representative cross sections through the lesion are shown by the vertical lines on the surface drawings. *R*, right hemisphere; *L*, left hemisphere.

nucleus medialis dorsalis to frontal cortex.¹¹ In addition, the nucleus ventralis anterior shows bilateral massive degeneration, sparing only its lateral border, and the nucleus ventralis lateralis has a zone of cell atrophy at the medial margin. Both these nuclei send fibers to the frontal cortex dorsal and caudal to the arcuate sulcus. As a result of the parietal damage, retrograde degeneration appears in the lateral portion of the

nucleus lateralis posterior and nucleus pulvinaris lateralis of Monkeys 1 to 4. The areas of cell atrophy in the latter nucleus are situated mainly at the dorsolateral portion and extend through the rostral two-thirds of its length. In some hemispheres, however, the degenerated zone includes also the ventral part of nucleus pulvinaris lateralis (i. e., both hemispheres of Monkey 2 and the left side of Monkey 4). In addition, the

RETENTION OF OVERLEARNED VISUAL HABIT

Number of Trials to Criterion for the Learning and Relearning of Visual Discriminations in Monkeys*

Monkey No.	Temporal Lobe Ablation											
	Preoperative			Post-Temporal			Prefrontal			Postparietal		
	I †	II ‡	III §	I	II	III	I	II	III	I	II	III
1	180	210	270	120	510	150	0	180	0	30	420	150
2	90	150	150	0	360	0	120	240	60	60	150	60
3	90	210	150	240	150	480	330	210	330	60	180	240
4	60	210	210	60	0	260	30	90	90	30	0	0
5	120	180	80	90	160	0						
6	210	210	180	30	60	270						
Control Animals												
	First Retention						Second Retention					
7	60	360	390	0	0	0	0	30	0			
8	330	330	210	0	0	0	0	30	30			

* Overtrained habits are set in italics.

† I. Red vs. green discrimination.

‡ II. Horizontal vs. vertical striations discrimination.

§ III. Diamond vs. disk discrimination.

nucleus ventralis posterolateralis of Monkey 4 shows cell atrophy, indicating the inclusion of the postcentral sensory cortex of the parietal lesion in this animal.¹² Graphic presentation of the thalamic retrograde degeneration in detail will be omitted here. The present results conform to the orderly spatial plan of individual thalamic nuclei projecting to the frontal, parietal, and temporal cortical areas, as reported by one of us previously.

Retention Tests of the Control Animals.

The accompanying Table gives the scores of the original learning and the retention tests of all subjects. Only the number of trials to criterion on each discrimination problem is listed. The error scores are comparable to trial scores; they need not be considered further. The two control animals (Monkeys 7 and 8) learned the original discriminations in from 60 to 390 trials. They showed perfect retention on all visual discriminations at the end of 6 weeks and, again, at the end of 12 weeks after the original training. Thus, normal monkeys do not forget visual discriminations either learned to criterion or overlearned beyond criterion after a period of three months. Therefore, any postoperative loss on these habits demonstrated in the experimental animals must be due to the cortical lesion and not to the time lapse itself.

Differential Effects of Temporal Cortical Ablation.—The six experimental subjects

(Monkeys 1 to 6) learned the three visual discriminations in from 60 to 270 trials preoperatively. Bilateral temporal extirpations affected these visual habits differentially. The Table summarizes the results. Four animals relearned the first problem, the red and green discrimination, with savings ranging from 100% to 33%. Monkeys 3 and 4 lost this habit and took at least the preoperative trials to reacquire it. The good retention shown by four out of the six experimental animals is rather unexpected. Our previous studies have repeatedly reported a loss of this habit in monkeys with temporal lobe removals.^{3,5,13} The experimental conditions of the earlier and of the present study are identical, except that the earlier animals were not given additional trials after criterion on any visual discrimination. Whether this overtraining on a pattern problem influences the postoperative retention of a color problem needs to be further investigated.

Of the two pattern discriminations, the six experimental monkeys showed various degrees of retention (ranging from 100% to 43% savings) on the one habit that was given an additional 500 to 1000 postcriterion trials. But all animals lost the other, not overtrained, pattern discrimination after the temporal cortical removals. They needed considerably more trials than the original learning to reacquire the not-overtrained habit (except that Monkey 5 took the same

number of trials as preoperatively to relearn the problem). Since the sequence of training and the specific pattern problems to be overtrained are balanced, the results obtained must be due to the fact that temporal cortical lesions have detrimental effects on pattern discriminations learned to criterion only, but not on overlearned visual habits.

Effects of Additional Frontal and Parietal Cortical Ablation.—After the completion of the post-temporal retraining, the four monkeys in experimental Group I were subjected to additional frontal and parietal cortical extirpations. Animals 1 and 2 had the frontal cortex removed prior to the parietal ablation, and Subjects 3 and 4, the parietal before the frontal operation. After each operation the animals were retrained to criterion on the three discriminations. The results are included in the Table.

With two exceptions, the animals retained the red-green discriminations (100% to 33% savings) after each of the two additional cortical removals. Monkey 2 lost this habit and took more than the number of preoperative trials to reacquire it after the second operation, on the frontal areas, and Monkey 3, after the third, frontal extirpation.

Differential effects on the two pattern discriminations similar to those following temporal lobe lesion again are apparent in the postoperative relearning scores of Monkeys 1 and 2. They retained the overlearned (100% and 60% savings) but forgot the other, not-overlearned, discrimination after frontal cortical extirpations. This contrasting result repeats itself for a third time subsequent to the two animals' last, additional, parietal cortical surgery. These findings indicate that the beneficial effect of overtraining a visual discrimination may spread from the temporal focus to regions other than the frontal and parietal areas. The fact that additional frontal and parietal cortical lesions cause the monkey to learn anew each time a not-overtrained habit suggests the vicarious functioning of these two cortical regions for visual discrimination

learning in the absence of the temporal neocortex.

The results obtained from the other two monkeys (Monkeys 3 and 4) in experimental Group I are in direct opposition. Animal 3 lost the overtrained and the not-overtrained pattern problems both after the second, parietal lobe removal and after the third, frontal cortex removal. After each additional operation, this animal used a number of trials either about equal to or more than the preoperative number to relearn each of the two discriminations. Monkey 4, on the other hand, retained both these two habits (100% to 58% savings) after each of the two additional cortical injuries. It would seem that the parietal and the frontal areas of Monkey 3 successively take over the visual function of the missing temporal cortex. But such function is sustained in Monkey 4 by areas other than the ablated parietal and frontal association areas.

Comment

The present results confirm the observation that temporal neocortical ablations affect the retention of visual habits trained to criterion only. After temporal lobe lesions, monkeys will lose a pattern discrimination trained to criterion but at the same time retain another pattern problem trained with additional hundreds of trials beyond criterion. These experimental findings may be compared with the clinical data that medial temporal lesions eliminate recent but not old memories. In either case, the possible neural mechanism responsible for such differential postoperative effects remains speculative. It has been shown previously that lesions in either the frontal or the parietal area do not affect the retention of visual discriminations learned to criterion in monkeys with intact temporal lobes.^{13,14} Thus, the neural substrate of visual discrimination is formed initially in the temporal cortex. As the training continues, or the habit becomes well ingrained, the neural changes must involve or spread to more and more additional cortical regions. Lashley's

concept of reduplicated patterns may suggest a mechanism for such neural spread from a focal point.

The behavioral effects after additional extirpations of frontal and parietal association cortices are not consistent in the present study. It seems that, at least for Monkey 3, both the frontal and the parietal association cortex participate in the preservation of the overlearned visual habit. This animal lost and reacquired the pattern problems after each of the two additional cortical ablations. The other three monkeys (Monkeys 1, 2, and 4) retained the overlearned problem throughout the three successive cortical insults, indicating the spreading of whatever neural changes to regions other than these association areas. Furthermore, both the frontal and the parietal area can function vicariously as the neural structure responsible for visual discrimination habits in the absence of the temporal lobe. Thus, three animals (Monkeys 1 to 3) lost and relearned a pattern problem trained to criterion subsequent to the ablation of either frontal or parietal cortex or both.

The present results on the red-green discrimination are unexpected. Contrary to earlier reports that temporal cortical ablations cause the monkey to lose this habit, four out of the six monkeys in this study retained this task after temporal operation. The animals also retained this habit with savings after the operation of frontal and parietal cortices. Only monkeys 2 and 3 lost and reacquired this task after their frontal removals. Since this problem is included as a preliminary adaptation process, the prolonged overtraining on a later pattern problem may eliminate the need of readaptation after surgery and hence account for the good retention.

The variations in the extent of the cortical lesions of the six experimental animals are probably not related to the variegated behavioral results discussed above. For example, the differential effect of temporal cortical lesions on the two pattern discriminations appear consistently in the six ex-

perimental animals. Yet the temporal lesions vary in size from the largest, in Animals 3 and 4, which includes large portions of superior temporal gyrus and the temporo-occipital region, to the smallest, in Monkey 6, which is confined to the central region of the middle temporal gyrus. Also, the largest parietal lesion is that of Monkey 4, and yet it is the only animal which retained all three visual discriminations after parietal surgery. The boundaries of the frontal lobe lesions are quite uniform in all four monkeys of experimental Group I, i.e., from the arcuate sulcus to the frontal pole. The right hemisphere of Monkey 3 is exceptional; its lesion includes the cortex ventral to the inferior limb of the arcuate sulcus. Whether this unilaterally enlarged frontal damage is responsible for the failure of Animal 3 to retain any one of the three discriminations after frontal operation is uncertain. This same animal also failed to retain both pattern problems after the preceding, parietal cortical extirpations.

Summary

Eight immature rhesus monkeys were divided into three groups: four animals in experimental Group I, two in experimental Group II, and two controls. They were trained first on a red and green color discrimination and later on two pattern discriminations: horizontal *vs.* vertical striations, and diamond *vs.* disk. All animals learned one of the two pattern problems to criterion only but overlearned the other pattern problem with either an additional 500 trials beyond criterion, as with the six monkeys in experimental Group I and the control group, or an additional 1000 trials, as with the two animals in experimental Group II. Both the order of presenting these two pattern discriminations and the choice of which discrimination was to be overtrained on which animal were balanced.

After bilateral temporal neocortical ablations all six monkeys in the two experimental groups retained the overlearned pattern discrimination but lost the other, not-overlearned pattern problem. They took

generally more than the preoperative trials to reacquire the latter. Four out of the six monkeys also retained the color discrimination.

The four monkeys in experimental Group I were subjected to two more cortical extirpations. Two of them had the frontal association cortex removed bilaterally prior to the bilateral ablation of the parietal association cortex. They retained the overlearned but lost the not-overlearned pattern habit subsequent to each of the operations. The other two monkeys had the parietal operation before the frontal surgery. One of them lost and the other retained the two pattern discriminations after each of the successive additional cortical removals. With two exceptions, the four monkeys showed repeatedly good postoperative retention on the color discrimination.

The two control animals showed perfect retention of the three discriminations tested after an interval of 6 weeks, and again after 12 weeks.

The anatomical findings on the cortical lesions of the experimental animals are reported. The extent of lesions was not related to the postoperative behavioral variations.

The possible neural mechanism necessary for the preservation of an overlearned visual habit following temporal cortical ablation, and the vicarious functioning of the frontal and parietal association areas on visual discriminations in the absence of the temporal cortex, are discussed.

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Newcastle Disease Encephalomyelitis in Cats

I. Clinical and Pathological Features

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It is difficult in man to study disease processes due to neurotropic viruses. However, certain clinical and "pathophysiological" abnormalities common to many of these diseases, such as seizures, myoclonus, or paralyses, may well be subjected to more precise study in laboratory animals artificially infected with viruses to which they are susceptible. Routes of infection can be chosen at will and the intensity to some degree controlled. It is the purpose of this and succeeding papers to describe some observations on cats following infection with Newcastle disease virus which may be relevant in interpreting analogous human disorders.

Newcastle disease virus is an epizootic infection of chickens characterized by viremia and signs of involvement of the respiratory, gastrointestinal, and central nervous systems. Doyle,¹ in England, first isolated a filtrable virus from a completely fatal endemic in Newcastle-on-Tyne and named the infection caused by this agent Newcastle disease. It has subsequently become apparent that this disease is widespread among chicken flocks the world over.

The virulent strain of Newcastle disease virus is neurotropic and, given orally, by

aerosol, or injected intramuscularly or intravenously, causes encephalitis in pigeons,² turkeys,³ ducks,⁴ and some wild birds.⁵⁻⁷ Intracerebral injection of this virus has produced encephalitis in hamsters,⁸ mice,⁹ cotton rats,¹⁰ and monkeys.¹¹ Mice¹² have been successfully infected by the intranasal route. In these reports are numerous descriptions of various disorders of movement, such as shivering, jerking, spasms of the head, neck, and body, twitching, torticollis, turning movements, and somersaulting.

The purpose of this first paper is to describe clinical, anatomical, and pathological features of Newcastle disease virus encephalomyelitis produced experimentally in cats. They provide basic information for the study of mechanisms underlying motor disorders, to be described in succeeding papers.

Materials and Methods

Of mammals successfully infected with Newcastle disease virus, most, with the exception of monkeys, do not lend themselves to detailed clinical follow-up, neuropathological correlation, or physiological studies. Accordingly, because of ready availability, and the wealth of existent neurophysiological information, cats were chosen for this investigation.

The virulent CG-strain of Newcastle disease virus was used. This strain was isolated from a natural outbreak of Newcastle disease in California by Beach in 1936. It has been maintained in this laboratory by approximately 36 allantoic passages. After inoculation, 10- to 11-day-old chicken embryos were incubated for 40-48 hours at 35 C. Stock virus was prepared by pooling allantoic fluid and storing it in 2 cc. ampules at -20 C. Virus dilutions were then freshly made as needed in 0.85% saline buffered at pH 7.2 with 0.01 M phosphate. From these, 0.05-1.0 cc. was used, depending on route of inoculation.

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Kittens and adult cats, weighing 0.5-4.0 kg., were chosen from stock. Only animals shown to be healthy by observation for at least two weeks were used. Blood was drawn by cardiac puncture for preinfection neutralizing antibody titers. All animals were then inoculated aseptically under pentobarbital or ether anesthesia by one selected route.

For intraneural infection, the proximal end of cut sciatic nerve was immersed in undiluted stock virus for 5-10 minutes. Intranasal exposure was achieved by dropping 0.25 cc. of undiluted virus into each nostril and hyperextending the animal's head for 5-10 minutes to allow adequate contact of the nasopharyngeal mucosa with the infective material. All other inoculations were through small needles. Intracerebral and intracerebellar injections, through burr holes, were made into the white matter of one frontal or of one/lateral cerebellar lobe, respectively. Intraocular injection was into the vitreous chamber of one eye. In these three situations, 0.1 cc. of virus dilution was regularly used. Lower cervical and midthoracic portions of spinal cord were injected under direct vision after appropriate laminectomy. Inocula in these regions were smaller—namely, 0.05 cc. of virus dilution. Intracardiac injections of 0.5-1.0 cc. of stock virus were made into the left ventricle. Subcutaneous inoculations were all into one lower extremity in quanta ranging from 0.5 to 1.0 cc. of virus dilution. The numbers of animals exposed through these various routes are shown in Table 1.

Animals developing Newcastle disease virus encephalomyelitis were studied clinically and, in many instances, photographed cinematographically and subjected to physiological experiment (succeeding papers). They were then anesthetized with intraperitoneal pentobarbital. After cutting the right atrium, they were perfused by gravity through the ascending aorta with 50-60 cc. of isotonic saline, followed by 800-1000 cc. of 10% formalin and 1% glacial acetic acid. The carcasses were then refrigerated at 4 C for 12-24 hours. Brain, spinal cord, and dorsal root ganglia, as well as stellate, celiac, and Gasserian ganglia, were removed and sectioned serially in celloidin. Sections were cut at 20 μ -30 μ , and every 30th section was stained with galloxyanin and with Greenfield's modification of phosphotungstic acid hematoxylin. Additional sections were stained in certain animals when a denser series was indicated. Lesions were plotted on serial drawings of coronal sections of cat brain, brain stem, and spinal cord.

Results

A. Relationship of Age, Route of Infection, and Dilution of Virus Inoculum to Development of Encephalomyelitis.—Kittens

and adult cats usually developed encephalomyelitis after direct intracerebral, intracerebellar, and intraspinal inoculation with Newcastle disease virus. Dilutions of stock virus out to 10⁻⁴ logs were effective by these routes. Adult cats, on the other hand, were apparently more resistant to infection by intranasal and intraocular injection than were kittens. Indeed, when these routes were used, successful infections were obtained only in kittens, and when inocula of undiluted or 10⁻¹ log dilutions of virus were used.

A total of 107 kittens and adult cats were exposed to the chick-adapted virulent strain of Newcastle disease virus. The number of animals inoculated by each experimental route is indicated in Table 1.

Of the total number of exposed animals, 53 developed signs and symptoms of Newcastle disease virus encephalomyelitis. Successful infection of central nervous system occurred only when the route was intracerebral, intracerebellar, intranasal, intraocular or into the spinal cord. Even with these routes no infection appeared in 27 animals observed for a period of 30-40 days after inoculation. Though indeterminate deaths occurred in some animals inoculated by intrasciatic, intracardiac, and subcutaneous routes, none of these or the remaining survivors developed signs of encephalomyelitis.

B. Clinical Signs of Newcastle Disease Virus Encephalomyelitis.—Encephalomyeli-

TABLE 1.—Results of Cat Inoculations with Newcastle Disease Virus

Route of Inoculation	No. Inoculated	No. Observed with NDV Encephalomyelitis	Survivals Without Signs	Indeterminate Deaths
Intracerebral	17	17	0	0
Intramedullary				
Cervical cord	14	9	0	5
Thoracic cord	7	7	0	0
Intracerebellar	4	4	0	0
Intraocular	10	7	2	1
Intranasal	19	9	8	2
Intrasciatic	12	0	6	6
Intracardiac	19	0	7	12
Subcutaneous	5	0	4	1
	107	53	27	27

NEWCASTLE DISEASE ENCEPHALOMYELITIS

TABLE 2.—Principal Signs of Newcastle Disease Virus Encephalomyelitis

Route of Inoculation	Mean Incubation, Days	No. Observed with Encephalomyelitis	Signs						
			Limb Paresis, %	Myoclonus, %	Convulsions (Focal and General), %	Head Tilt, %	Cranial Nerve Palsies, %	Salivation, %	Nystagmus, %
Intracerebral	3-4	17	88	82	12	41	6	0	12
Cervical cord	2-3	9	100	88	0	33	0	0	0
Thoracic cord	4-5	7	100	71	0	0	0	0	0
Intracerebellar	3-4	4	100	100	0	50	0	0	0
Intraocular	17	7	70	70	28	0	43	43	0
Intranasal	11	9	66	55	66	66	22	0	11

tis followed intracerebral, intracerebellar, and intra-spinal-cord inoculation of adult cats and kittens after incubation periods averaging three to four days. In kittens infected intranasally signs of illness occurred only after 11 days or more. With intraocular inoculation, incubation was even longer—an average of 17 days. In all groups, however, the clinical picture of encephalomyelitis was similar. Its sequence varied only with the anatomical site of primary infection.

It was seldom that animals showed any change in vigor, activity, or appetite prior to development of neurological abnormalities. Not infrequently, on either the day preceding or the actual day of onset of signs there was moderate to marked temperature elevation. From this time onward the course was fulminating. Terminal drop in temperature and death usually occurred in 12-48 hours from onset of the first clinical indication of central nervous system involvement.

The principal neurological abnormalities observed in cats with Newcastle disease virus encephalomyelitis were paretic and convulsive, as indicated in Table 2. Consciousness was preserved until the terminal stages. Indications of mental aberrations, as noted below, were few.

1. The convulsive disorders were distinctively of three main types, emerging in stages as follows:

(a) In animals inoculated by intracerebral, intracerebellar, intranasal, and intraocular routes, neurological abnormalities developed in a similar sequence. Commonly, head tilt to one side or the other was the

first sign of central nervous system involvement. This was succeeded in a few hours by onset of involuntary rhythmic myoclonus of the head, neck, trunk, and extremities. The rate varied from 40 to 130 per minute, regardless of site of inoculation. It progressively increased during the course of the illness. The rhythm could be altered by repetitive low-frequency auditory stimuli, such as hand clapping. This myoclonus evolved in a cephalocaudal direction, affecting successively the head, neck, forelimbs, trunk, lower limbs, and tail, and persisted throughout the illness. In most animals it was bilaterally synchronous and symmetrical, though in some instances it began in one upper limb, then became bilateral.

When virus was injected into the cervical or thoracic spinal cord, the clinical picture was somewhat different. In the cervical group myoclonus first began in the upper extremities and later spread to the lower segments. In cats with inoculation of the thoracic cord myoclonus first developed in the lower trunk and lower limbs. Only later, and to a less degree, were forelimbs, neck, and head involved.

(b) Concurrently, or later, in some animals, sustained extensor spasms of the head, neck, and upper extremities with fanning of toes occurred. These spasms lasted several seconds, recurring every few minutes.

(c) Terminally, in a few animals, there were frank focal or generalized convulsions.

2. Weakness was a prominent symptom. It occurred in the upper and lower limbs and had the characteristics of a lower motor neuron disorder, with flaccidity and dimin-

ished or absent deep tendon reflexes. At onset the weakness was usually limited to one limb. With passage of time, however, it usually spread progressively to involve other extremities, and even the trunk. In terminal stages nearly all animals were prostrate.

Cranial nerve palsies, oftenest observed in the animals infected intraocularly, were less frequent than limb and trunk weakness. Of these, pupillary abnormalities, especially anisocoria, and facial palsy were the most commonly recognized. Later, in some animals, constant salivation was interpreted as evidence of bulbar palsy.

3. Progressive disturbances in postural and vestibulo-ocular mechanisms were not unusual. Head tilt became more pronounced. Many animals in the first and subsequent days of illness exhibited circling movements, and some, frank somersaulting. Horizontal nystagmus was seen in two animals.

4. Detectable mental changes, other than those commonly seen in any acutely ill animal, were exceptional. When present, they were limited to animals inoculated by the intracerebral, intranasal, intraocular, or intracerebellar route. They consisted of growling, hissing, piloerection, and purposeless repetitive striking and clawing movements. For the most part, these behavioral aberrations were manifest only when the animal was disturbed.

C. Pathological Features of Newcastle Disease Virus Encephalomyelitis.—Serial sections of brains and spinal cords of cats with Newcastle disease virus encephalomyelitis were examined and compared with those from control animals. The number of brains thus examined after infection by different routes are listed in Table 3.

TABLE 3.—Route of Inoculation and Number Examined Histologically in Serial Section

Route of Inoculation	No. Brains and Cords Serially Examined
Intracerebral	2
Intranasal	5
Intraocular	4
Intracerebellar	2
Cervical cord	5
Thoracic cord	4
Subtotal	22
Controls	2
Total	24

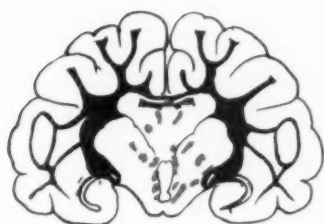
Except for lesions in the olfactory cortex in the nasally infected group, and an occasional cat with meningitis, the cerebral cortex was essentially normal. The pathological changes were found elsewhere. They consisted of certain local primary lesions characteristic of the route of infection, and others common to all the animals (Fig. 1).

In the intranasal group, cuffing of blood vessels, glial nodules, and focal inflammatory changes were prominent in the olfactory bulb (Fig. 2*A*) and tract, the piriform and preoptic areas, and the fornices. Certain related gray centers showed similar lesions. These were the amygdaloid nuclei, paraolfactory and septal areas, cornu ammonis, midline thalamus, and hypothalamus. Although damage was generally bilateral, the brain of one cat in this group showed predominant inflammatory changes involving the right primary and secondary olfactory areas. The spread of lesions remained unilateral as far back as the midline nuclei of the thalamus and the hypothalamus (Fig. 2*B*). At the lower level of the midbrain tegmentum, however, this unilateral predominance was no longer apparent, and caudally from here there was symmetrical involvement of brain-stem tegmentum (Fig. 3*A*).

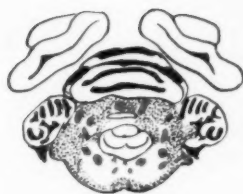
Fig. 1.—Representative coronal sections of the cat's central nervous system to show the distribution of lesions, indicated by red dots, of Newcastle disease virus encephalomyelitis after intranasal infection. Lesions of cerebral cortex were limited to secondary olfactory areas, and those of cerebellum to roof nuclei of the fourth ventricle. Lesions were widespread in the tegmentum of the brain-stem centers, involving particularly the red nucleus, vestibular nuclei, and reticular formation. Later, there was spread to the gray matter of the medulla and spinal cord. By other routes of inoculation, caudal or rostral spread along these same preferential pathways was dependent on site of inoculation.



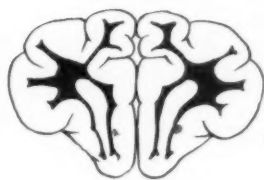
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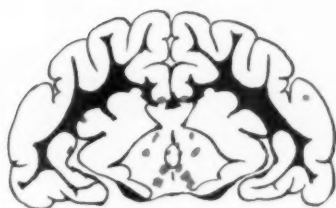
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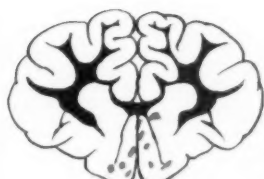
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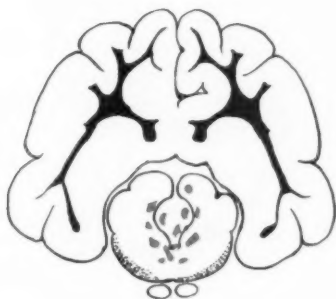
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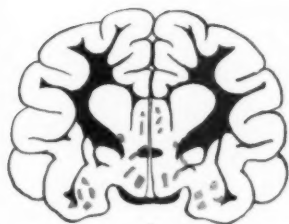
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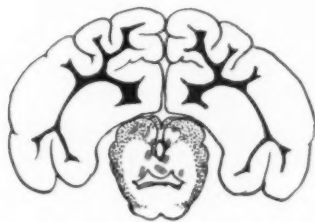
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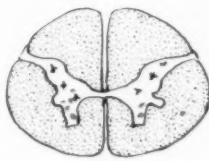
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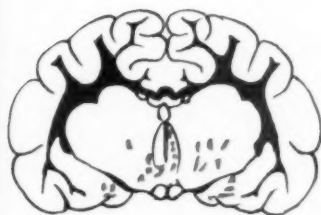
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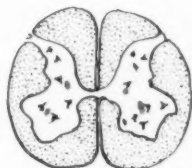
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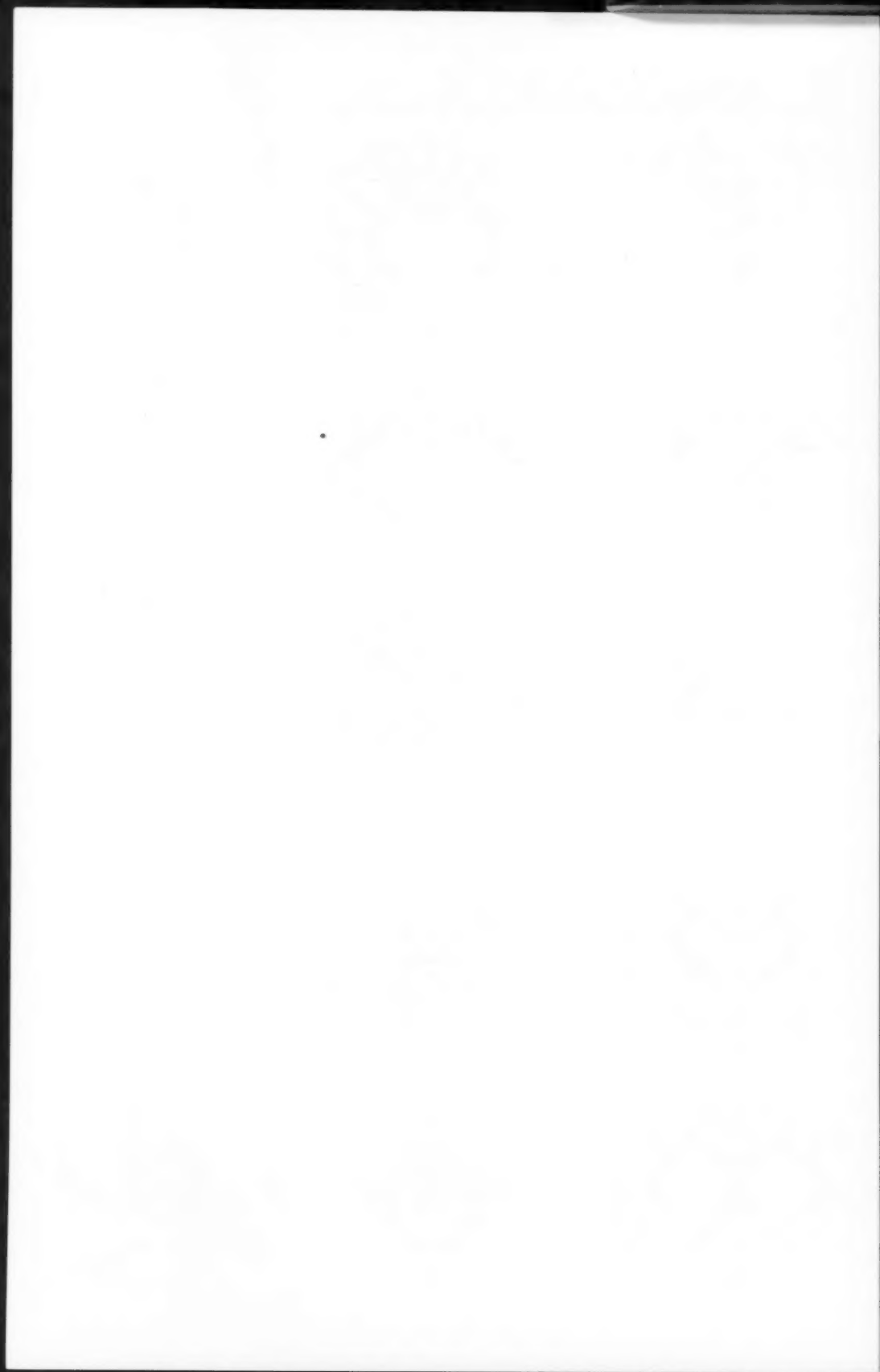




Fig. 2.—*A*, coronal section through the olfactory bulbs to show a glial nodule above, between the olfactory nerve and the glomeruli. Intranasal infection. Galloxyanin stain; $\times 50$.

B, coronal section through cerebral hemispheres and midbrain to show perivascular cuffing, glial nodules, and diffuse inflammatory changes of tegmentum at the level of the red nucleus, substantia nigra, and oculomotor nuclei. The involvement is more intense on one side than on the other. Intranasal infection. Galloxyanin stain; $\times 3.8$.

The intracerebral group, on the other hand, showed a necrotizing reaction at the site of inoculation. The lesions spread thence to the midline thalamic nuclei and

hypothalamus. It was of considerable interest that in animals inoculated intraocularly few abnormalities were found rostral to the brain stem.

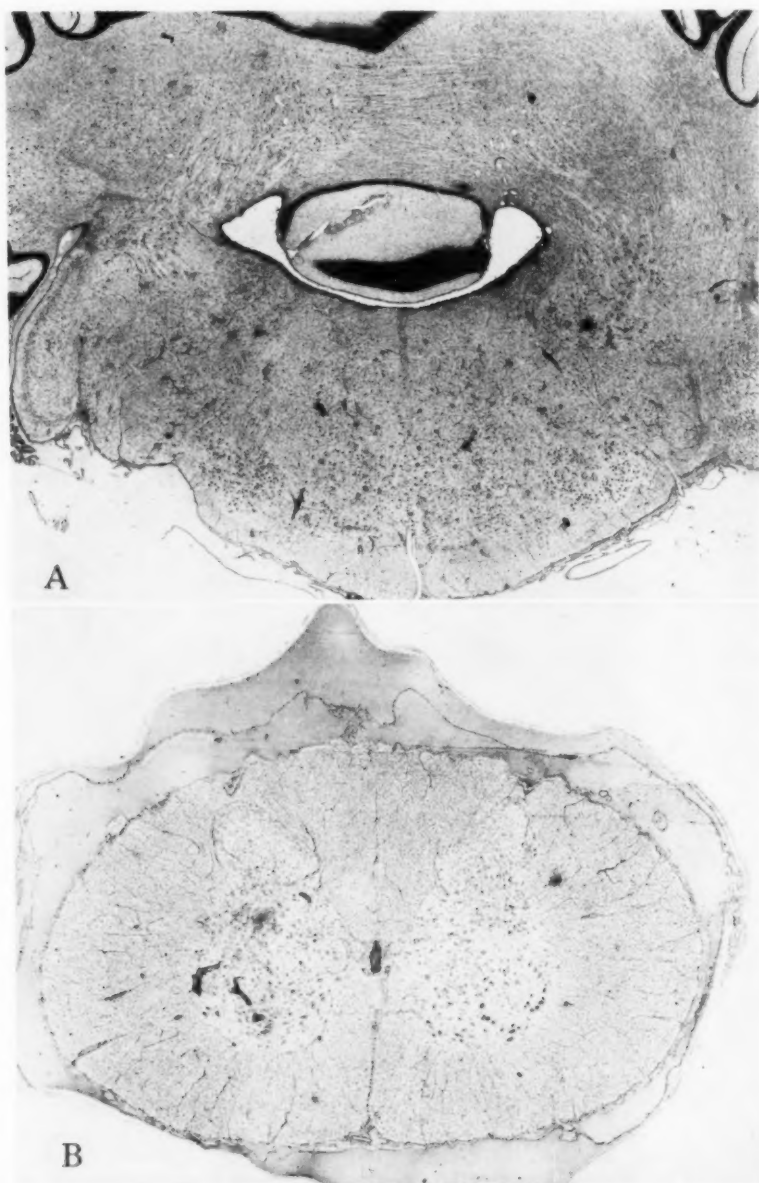


Fig. 3.—*A*, coronal section through the pons and fourth ventricle to show perivascular cuffing, and focal and diffuse inflammatory changes in the region of the vestibular nuclei, reticular formation, and basal cerebellar nuclei. The involvement is equally intense bilaterally. Intranasal infection. Galloxyanin stain; $\times 10$.

B, coronal section of the spinal cord through the cervical enlargement to show intense perivascular cuffing, focal and diffuse inflammatory changes, and destruction of anterior horn cells. The lesions are much severer on one side than the other. An occasional glial nodule is present in the white matter. Intranasal infection. Galloxyanin stain; $\times 20$.

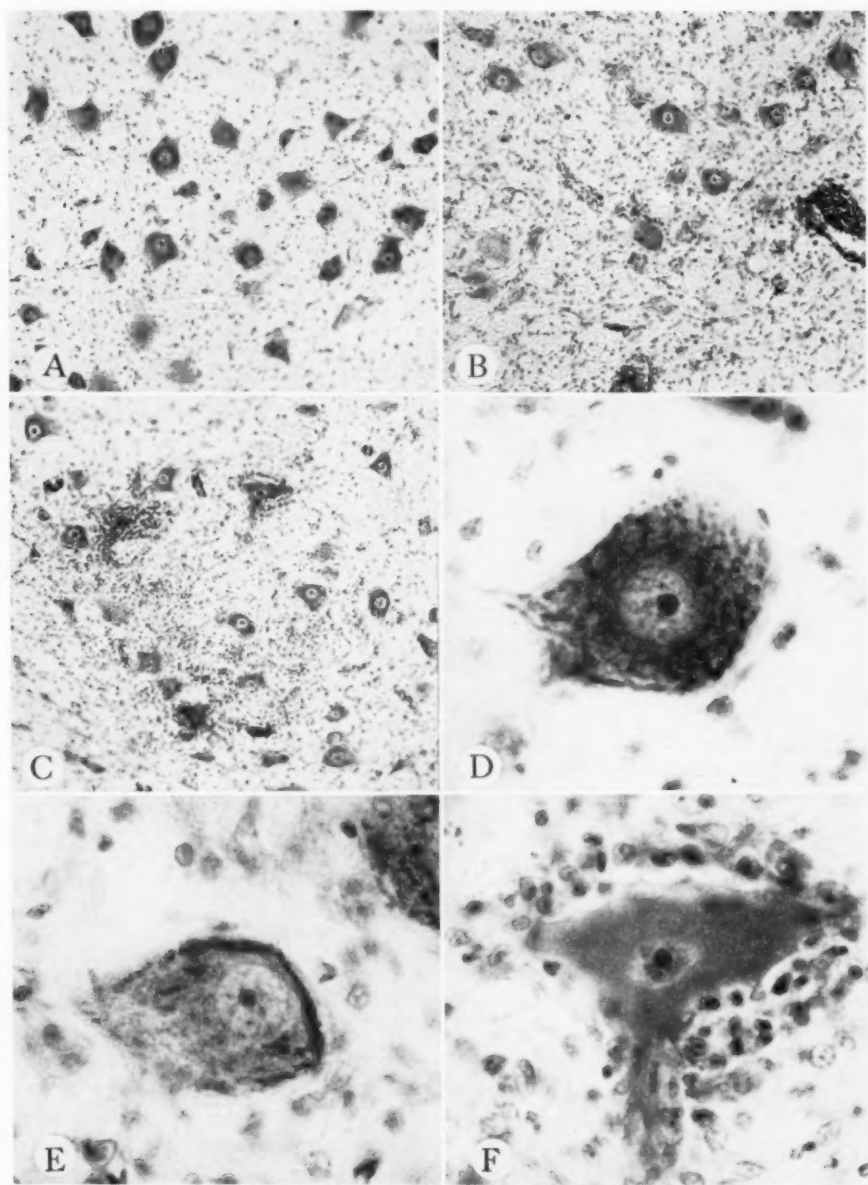


Fig. 4.—*A*, nucleus ruber. Control. Galloeyanin stain; $\times 100$.
B, nucleus ruber to show early chromatolysis and intense perivascular cuffing. Intranasal infection. Galloeyanin stain; $\times 100$.
C, nucleus ruber to show satellitosis, neuronophagia, diffuse inflammatory changes, and more advanced chromatolysis. Intranasal infection. Galloeyanin stain; $\times 100$.
D, cell from nucleus ruber. Control. Galloeyanin stain; $\times 600$.
E, cell from nucleus ruber to show early chromatolysis with margination of the Nissl substance. Intranasal infection. Galloeyanin stain; $\times 600$.
F, cell of nucleus ruber to show intense satellitosis, advanced chromatolysis, and pyknosis of the nucleus. Intranasal infection. Galloeyanin stain; $\times 600$.

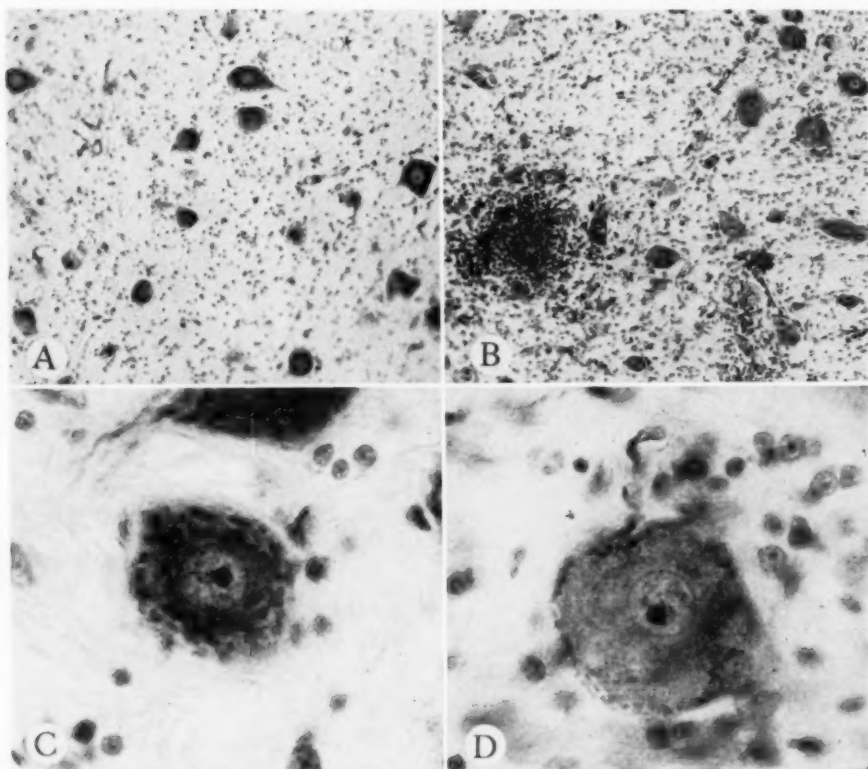


Fig. 5.—*A*, nucleus vestibularis spinalis. Control. Gallocyanin stain; $\times 100$.
B, nucleus vestibularis spinalis to show glial nodule, diffuse inflammatory reaction, satellitosis, and early chromatolysis. Intranasal infection. Gallocyanin stain; $\times 100$.
C, cell from nucleus vestibularis spinalis. Control. Gallocyanin stain; $\times 600$.
D, cell from nucleus vestibularis spinalis to show moderately advanced chromatolysis. Intranasal infection. Gallocyanin stain; $\times 600$.

In all three groups, the spread, thereafter, followed a common caudally extending pattern. In succession, there was involvement of the tegmentum of the brain stem, with ganglion cells of the red nucleus (Fig. 4), substantia nigra, medial and lateral vestibular nuclei (Fig. 5), basal cerebellar nuclei, and reticular formation showing varying degrees of chromatolysis, satellitosis, and neuronophagia. Cranial nerve nuclei were also damaged to some degree. Finally, diffuse and focal inflammatory changes with neuronal damage appeared in the gray matter of the cord. Here, though not limited to any particular area, damage

was usually greatest in the midzones and anterior horns (Fig. 3*B*).

In contrast, following cerebellar infection, spread of lesions was in a rostral direction. The same pathways and nuclei were involved in the common extension described in the other groups, only the direction was reversed. Lesions in one of these animals progressed as far forward as the piriform and septal areas.

Comment

Through the use of controlled means of infection and careful neuropathological studies, Bodian and Howe^{13,14} showed dis-

semination of poliomyelitis virus along preferential neuronal pathways, with involvement of susceptible nuclei of the brain, brain stem, and cord. In essence, that has been the approach of the present investigations. Newcastle disease virus, naturally occurring in poultry epidemics, has been successfully transferred to a larger mammal, with resultant encephalomyelitis. The broad features of the illness are similar in chickens and in cats, but the latter have the distinct advantage of lending themselves to more careful clinical observation and physiological study.

Here, too, as in poliomyelitis, once the infective agent gained access to the central nervous system, it seemed to follow a definite preferential pattern in its spread. For various reasons, the most cogent of which is the anatomical distribution of lesions, it has seemed that the primary pathways at least are neuronal in nature rather than the spread being by contiguous diffusion, and that to some extent the agent is disseminated along neurons within functional units. For example, in intranasally inoculated animals, there is clear evidence of extension along olfactory pathways and their secondary centers to deeper structures of the thalamus and hypothalamus. Below these levels, and particularly below the midbrain, the neuronal basis for dissemination is less clear. It might, indeed, be suggested that the consistent bilaterality of nuclear lesions in the midbrain tegmentum, reticular formation of the hindbrain, and gray matter of the medulla and spinal cord was contradictory to that explanation and that free contiguous spread was more probable. On the other hand, the striking symmetry of damage to paired nuclear structures, such as the red nucleus, oculomotor centers, substantia nigra, and vestibular and basal cerebellar nuclei, suggests strongly preferential routes of communication between them. By strong inference, this restricted mode of virus spread is neuronal. Indeed, a similar explanation, namely, the use of preferential nuclear and internuclear decussating path-

ways, was advanced by Bodian and Howe¹³ for the dissemination of poliomyelitis virus.

Again, it is difficult to postulate a means of virus extension other than neuronal to account for the interesting sequence of lesions resulting from inoculation of cerebellum and cervical spinal cord. From these sites the spread was predominantly rostral and involved the same susceptible regions and nuclei, and even extended in some instances up into the secondary olfactory pathways. In these animals infected from the more caudal sites, however, death was clearly earlier after onset of illness than in those inoculated intracerebrally and intranasally. As a consequence, perhaps, inflammatory and neuronal changes in the brain stem were less advanced when examined histologically. At any rate, it is clear that destructive changes leading to death were not entirely commensurate with the visible pathological changes.

The mechanisms underlying myoclonus, such as were exhibited by these animals, have been little understood. Indeed, even common sites of lesions resulting in analogous rhythmic involuntary movements in man are far from defined, although myoclonus has frequently been described in humans with certain suspected viral infections. Von Economo,¹⁵ for example, described extensive brain-stem damage in his myoclonic patients with a "poliomyelitic form of encephalitis lethargica." Van Bogaert, Radermecker, and Titeca,¹⁶ in their study on myoclonus, distinguished two clinical types. The myoclonus obtained in the present animal experiments is of the type they associated with lesions in the subcortical regions of the forebrain. More recently, however, Campbell and Garland¹⁷ have extended the range of possible sites for myoclonus elaboration in presumed virus infection by presenting evidence that it may occur purely at the spinal level. In the experiments reported here, the myoclonus could most readily be correlated with lesions either of the brain stem or of the spinal cord. Several

animals infected by intraocular or intracerebellar routes developed myoclonus and showed lesions confined to the brain stem. Within that region the red nucleus, substantia nigra, vestibular nuclei, and gray matter of the reticular formation were always the areas most severely involved. On the other hand, lesions were limited to the gray matter of the spinal cord in certain other animals which had demonstrated equally prominent myoclonus after spinal inoculation. Indeed, it may well be that the excitatory effect of this virus, and perhaps other viruses, may exert itself at any level of the central nervous system. If such is true, the complexity of the particular rhythmic outburst would be limited only by the degree of organization at that level.

It is tempting to carry over features from this laboratory infection to theoretical considerations of certain encephalomyelitides encountered in man. In this sense, the syndrome of myoclonus and limb paresis, and the general anatomical distribution of lesions due to Newcastle disease virus in cats, are similar to von Economo's "hyperkinetic-poliomyelitic form" of encephalitis lethargica. The causative organisms behind the latter remain unknown largely because methods of virus isolation, complement-fixation tests for viruses, and tissue-culture facilities were not then available. Fortunately, cases of encephalitis lethargica are now sporadic, and, indeed, even rare. Should the disease recur in endemic or epidemic proportions, it might well be advisable to search carefully among members of the myxovirus group for causative organisms.

Summary

Kittens and adult cats were successfully infected by several routes with chicken-adapted Newcastle disease virus. The clinical features of the resultant encephalomyelitis are described and were similar to those observed in the chicken.

The use of controlled means of infection and neuropathological study showed that once this virus gained access to the central

nervous system it seemed to be disseminated along preferential neuronal pathways, and to some extent along neurons within functional units.

The clinical phenomena of myoclonus and limb paresis and the general anatomical distribution of lesions bore a resemblance to those in von Economo's "hyperkinetic-poliomyelitic form" of encephalitis lethargica. Experiments reported here suggest that myoclonus in these cats with Newcastle disease virus encephalomyelitis resulted from some "pathophysiological" change occurring at either brain-stem or spinal-cord level.

Room 403, Osler Building, The Johns Hopkins Hospital.

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News and Comment

ANNOUNCEMENTS

American Board of Psychiatry and Neurology, Inc.—It is the intention of the American Board of Psychiatry and Neurology, Inc., to undertake special foreign certification of physicians who are not residents of the United States or Canada, not holding licensure for the practice of medicine in those countries, and not contemplating medical practice in those countries, by a certifying examination after completion of prescribed requirements. For details and regulations, write Dr. David A. Boyd Jr., secretary-treasurer, American Board of Psychiatry and Neurology, Inc., 102-110 Second Avenue, S. W., Rochester, Minn.

Training Fellowship.—New York University-Bellevue Medical Center is offering a three-month training fellowship with stipend in neuroanatomy and neurophysiology, beginning September, 1958.

For information apply to Dr. Louis Hausman, Department of Anatomy, New York University-Bellevue Medical Center, 550 First Ave., New York 16.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Abner Wolf, M.D., President, New York Neurological Society, Presiding
Joint Meeting, Jan. 8, 1957

Some Observations on Soviet Neurology and Psychiatry. DR. STANLEY LESSE.

The material for this report was gathered during a visit to the Soviet Union in June and July, 1956. Clinical neurology and psychiatry in the U. S. S. R. are under the control of the Ministry of Health, while research is directed by the Ministry of Health, the Academy of Medical Sciences, and the Academy of Sciences. The Russians present statistics which they state back their claims that psychiatric illnesses are not a major problem in the U. S. S. R. However, their statistics must not be accepted at face value because of the cultural differences and differences in diagnostic criteria. They stress the avoidance of psychiatric hospitalizations by acute treatment centers, called *Stationsars*, where intensive organic therapy and psychotherapy may be given to acutely disturbed patients. Sleep therapy, according to Pavlov's concepts of "protective inhibition," is stressed.

Neurologic and psychiatric research is dominated by the concepts and theories of Pavlov. The so-called "second signal system" is a higher phase of conditioned-reflex research that is prominently discussed at this time.

Discussion

DR. ABNER WOLF: I congratulate Dr. Lesse on the volume and quality of information that he was able to accumulate in such a short period of time. His paper is open for discussion.

DR. PHILIP R. LEHRMAN: I have talked to Dr. Lesse privately, and I may as well say it publicly: When I was in Russia in 1936, I, too, observed many alcoholics in their parks of rest and culture; I also observed that social phenomenon which they deny having: prostitution. At that time, in Moscow, I visited the last prophylactorium which was in the program to liquidate the problem of prostitution. The treatment was really phenomenal. Those girls were first of all examined medically, neurologically, and psychiatrically, and then they were inspired to learn a trade, which was taught them at this prophylactorium. The doctor in charge was Professor Andreyev.

The problem of psychoanalysis in the U. S. S. R., as you may all know, was solved in 1928 by a decree that "no more paper was available for publication of psychoanalytic books." That followed the publication of Freud's "The Future of an Illusion," in which Communism was compared to the doctrines of the church. As you may gather, that was not altogether agreeable to the regime, and so "no more paper was available for publications on psychoanalysis." However, I sought out one psychoanalyst (I do not know how politic it would be to mention his name, and I shall not do so), who talked to me very privately and confidentially about what went on. This psychoanalyst was at that time very busy psychoanalyzing the children of some of the highest officials! The psychoanalyst, however, could not teach psychoanalysis, nor were there any training facilities for younger people to learn this discipline. I have asked Dr. Lesse privately whether he met any of these people, and he told me he had not. I was much interested in hearing Dr. Lesse's paper and think it is a worthy contribution to our knowledge of what goes on.

DR. MORRIS HERMAN: Dr. Lesse, were you able to see the collection of journals and books in these institutes, and do they include psychoanalytical journals, even if not printed in Russia? From how many languages are their journals translated?

DR. STANLEY LESSE: I shall answer the second question first. Within approximately two months of the publication of a journal in this country it is available in the Soviet Union, and already translated and spread over all the large research centers; within two months they have our literature there.

DR. MORRIS HERMAN: Including analytical material?

DR. STANLEY LESSE: I cannot answer that specifically, but I do know that in the translations of a few books that I have read the authors certainly appeared to know the psychoanalytic literature.

As to the number of languages: English is the language being stressed now in the Soviet Union. As the head of one of the institutes said, "There

are only two languages in the world right now: English and Russian." At one time French was the language of culture. They had some people in the institutes, between 60 and 70 years of age, who would speak French. German is also commonly known, but the young people are all studying English.

There is one other point I would like to mention to show how much is being invested in medicine. They are turning out 26,000 doctors a year as compared with about 8000 in this country. They are saturating the communities with doctors. Their course is a six-year one. They do not have pre-medical courses of the kind we have over here.

I should like to say one more thing in conclusion: I feel they know a great deal of what we are doing because they have our literature. The American journals, as I said, are available in the Soviet Union two months after their appearance here. We do not know very much of what they are doing. I think this is a mistake. Hypothetically, even if much of their research is found to be of limited value, where there are so many thousands of people doing research, it would be a mistake for us to overlook their findings. I think it would be a great help to us to have a greater number of translations of their literature made easily available to us for our general surveillance.

DR. ABNER WOLF: In relation to Dr. Lesse's last remark, I would like to point out that a recent number of *Science* took up this problem of the translation of Russian literature, and some arrangement is being made with the English to divide the translation between them and us, so that journals will become promptly available.

Pathogenesis of the Diabetes Insipidus That Follows Total Hypophysectomy in Man.

DR. F. STEPHEN VOGEL (by invitation).

Variable degrees of persistent polyuria and polydipsia have been manifest in patients following total hypophysectomy for carcinoma (Pearson, O. H., et al. *J. A. M. A.* 161:17, 1956. Lipsett, M. B., et al.: *J. Clin. Endocrinol.* 16:183, 1956). In consideration of the pathogenesis of the diabetes insipidus, attention was given to the possibility that alterations might exist in the cells that normally form the antidiuretic hormone, namely, those of the supraoptic and paraventricular nuclei and, also, to the possibility that the residual infundibular tissues might not adequately assume the functions of storage and transfer of the hormone from the neural tissues to the blood stream, as performed by the posterior lobe of the pituitary, prior to hypophysectomy. Serial sections of the hypothalamus of 13 patients, 8 days to 16 months after total hypophysectomy, regularly showed marked cytologic changes in the supra-optic and paraventricular nuclei. These were

characterized early as a liquefaction necrosis, and later as a dropping out of cells with gliosis. They were ascribed to a retrograde degeneration of the neurons. The residual infundibular stalk regularly showed gliosis, often with thrombosis and occlusion of many portal, capillary blood vessels, and as a rule contained scant amounts of antidiuretic hormone, that was stainable by Gomori's chrome alum, hematoxylin-phloxine method. In general, in individual cases, a reasonably close correlation existed between the degree of diabetes insipidus and the degree of cytologic change in the supraoptic and paraventricular nuclei, when considered together with the quantity of hormone and the degree of change in the infundibulum.

Discussion

DR. ABNER WOLF: This fine demonstration by Dr. Vogel of the effects on the hypothalamic nuclei of surgical excision of the pituitary is in consonance with those that have been observed in experimental work on lower animals, and aids in our understanding of the problem of diabetes insipidus. I should like to ask one question: Was the point of separation, or incision of the stalk of the pituitary, close to the infundibulum, or low down, near the pituitary?

DR. F. STEPHEN VOGEL: In most cases the stalk of the pituitary had been severed at approximately the junction of the middle and the upper third.

DR. ABNER WOLF: I see Dr. Pool is here; he has done some hypophysectomies, and perhaps he would care to join the discussion.

DR. J. LAWRENCE POOL: I have done only five hypophysectomies for carcinomatosis, and all the patients developed diabetes insipidus postoperatively. We attempted a hormonal assay of the blood and fluid obtained from the infundibulum by constant gentle suction through a small plastic catheter after sectioning the pituitary stalk. Perhaps this may have contributed to the retrograde neuronal degeneration you, Dr. Vogel, have described so beautifully. Let me congratulate you warmly on this careful work, which is of such great interest and value.

DR. ABNER WOLF: I wonder whether cutting the pituitary stalk as close to the gland as possible would tend to spare the infundibulum and permit it, as far as is possible in man, to take over the storage function of the posterior lobe.

DR. F. STEPHEN VOGEL: That would seem reasonable.

DR. ABNER WOLF: Is there any possibility of revascularization of the infundibulum after operation that might serve to preserve what function it has?

DR. MORRIS HERMAN: One thing is not clear to me: You pointed out the granules in the fibers

coming down the stalk. Is it the implication that they traverse that path, or is there a venous portal circulation that was not mentioned in which they travel between the supraoptic nuclei and the posterior lobe of the pituitary?

DR. F. STEPHEN VOGEL: There is no vascular channel which connects the supraoptic nucleus directly with the posterior lobe of the pituitary. The droplets of antidiuretic hormone lie next to the nerve fiber—not in the fiber, but adjacent to it. What space they are in I am not prepared to say.

DR. ERICH G. KRUEGER: There is one thing that should be mentioned: Dr. Bronson Ray indicated to us that he encountered these 13 cases of diabetes insipidus in the beginning of his series of hypophysectomies, when he was still in the habit of cauterizing the pituitary stalk. There was, as nearly as I recall, no incidence of diabetes insipidus after he omitted electrocautery when dissecting the pituitary stalk.

DR. F. STEPHEN VOGEL: The cases discussed this evening were from Dr. Ray's service.

Perception Experiments in a Study of Ambivalence. DR. SIDNEY TARACHOW, DR. HYMAN KORIN, and DR. STANLEY FRIEDMAN (all by invitation).

This perception experiment is part of a larger study, in which we attempt to correlate certain specific aspects of opportunities for object relations in early life with success or failure in the fusion of ambivalent tendencies. This study presents the correlations of two of our attempted measurements of the fate of the ambivalence. One measurement is a structured interview which classifies subjects according to ego efficiency and organization, and the other measurement is a tachistoscopic visual test in which we measure the accuracy of initial perception, the degree of recovery of preconscious perception, and the nature, quality, and range of the subsequent imagery which can be elicited from the subjects.

Our hypothesis concerning the relationship of the tests is that there is a relation between the efficiency of ego functioning and the range of imagery which can be elicited. The greater the impairment of integrative and defensive ego functioning is, the wider will be the range of imagery: These two are related to impairment of fusion of ambivalent tendencies.

The data were consistent. Of 29 psychoneurotic subjects, either inpatients or outpatients at Hill-

side Hospital, those classified as having severe disturbances in ego functioning had, as compared with those with low disturbance in ego functioning, more correct perception of both aggression and sex in the stimulus picture; better human quality, better detail, and better affective quality in their drawings; better recovery of preconscious percepts, and a wider range of imagery. This work serves as a control on the original work of Poetzl (*Ztschr. Neurol. u. Psychiat.* 137:278, 1917) and the recent work of Fisher (*J. Am. Psychoanal.* 4:5, 1956), which demonstrated the existence of preconscious perception in tachistoscopic experiments and the recovery of these percepts via dreams or imagery. Our work indicates that perception and range of imagery vary with the degree of damage to ego organization and with the fate of the fusion of ambivalence.

Discussion

DR. JOOST A. M. MEERLOO: One can use the function of discussion of a paper to rid oneself of personal ambivalences by criticizing slight omissions, or one can try to find modulations and free associations with a common theme of interest. I hope to limit myself to the latter pleasant task.

The research project of Dr. Tarachow and his collaborators on experimental data on ambivalence is important, because this neglected subject in psychiatry asks for a multiple approach if one is to understand the contrasting tendencies and ac-

This research project on ambivalence is a significant step toward integration of clinical, psychoanalytical, and psychotechnical concepts.

WALDIMIR G. ELIASBERG: The problem which Dr. Tarachow and his co-workers have tackled with their tachistoscopic experiments has been a central one in philosophy since Leibnitz, in psychology since the introduction of the tachistoscope, and in psychopathology since the time when one started to interpret clinical phenomena on the basis of experimental psychological data. It was Leibnitz who described the inner "affairs" of the monads as perceptions, and particularly petite perceptions, as mathematical differentials of consciousness, as hardly noticeable subconscious events.

Dr. Tarachow has hit on one of the central problems of psychology and psychopathology. It remains to be seen whether his results can be completely grasped in the concept of ambivalence.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Diseases of the Spinal Cord

NEOPLASTIC DISEASE OF THE SPINAL EXTRADURAL SPACE. J. MULLAN and J. P. EVANS, A. M. A.
Arch. Surg. 74:900 (June) 1957.

Fifty patients with spinal extradural tumor were treated by laminectomy and postoperative irradiation. Good results were obtained in 32% of the patients; 26% were moderately improved, and 28% were considered failures. Causes of failure were due to the degree of malignancy, severe cord damage, and errors of judgement and technique. There were 14 cases of neoplasm locally destroying the bone, such as hemangioma, hemangioendothelioma, pericytoma, giant-cell tumor, chondrosarcoma, and lipomyxosarcoma. In general, these lesions showed satisfactory responses.

Among 15 cases of reticular tumors, those of Hodgkin's disease and lymphosarcoma responded well to treatment, but the myelomas and reticulum-cell sarcomas gave disappointing results. Twenty-one patients with metastatic tumor of the spine did poorly, with complete failure in eleven cases.

The authors advise early use of myelography, whenever extradural tumor of the spine is suspected. If the anatomic nature of the lesion is unknown, primary radiotherapy should be given only when the signs of cord compression are minimal or absent. As a rule, immediate decompressive laminectomy is indicated in all cases in which the spinal cord is compressed. The histologic type and radiosensitivity of the tumor are unknown. The longer a total paraplegia exists, the less favorable are the chances for functional recovery; yet in a single instance paralysis of two months' duration was improved by laminectomy. Secondary operations are useless. In the future, the results are likely to be improved and the failures reduced to one-third of the present figure of 28%, provided the diagnosis of extradural tumor is made earlier and the treatment instituted before the paraplegia develops.

LIST, Grand Rapids, Mich.

HERNIATED LUMBAR INTERVERTEBRAL DISKS. H. G. DECKER and S. W. SHAPIRO, A. M. A.
Arch. Surg. 75:77 (July) 1957.

Decker and Shapiro report their experiences with 347 patients who were explored for lumbar herniated disk. A ruptured disk was found in 279 cases, intraspinal neoplasm in 3, and other pathology causing root compression in 13. In the remaining 52 cases exploration revealed no cause for the clinical symptoms. Five per cent of the patients with ruptured disk had no back pain, and 2% had only back pain but no root irritation. The disk ruptures occurred at the L5-S1 level in 59.4%, at L4-L5 in 37%, and at higher lumbar levels in only 3.6%. In the authors' opinion, the level of the ruptured disk cannot be accurately determined by clinical methods; for example, the weakness of the toe extensors, which supposedly characterizes the herniation at the level of L4-L5, was found with equal frequency with herniation at other levels; however, the ankle reflex was most frequently abolished in cases of ruptured lumbosacral disk. Narrowing of the L4-L5 interspace on ordinary x-rays proved of some diagnostic value, whereas a reduced lumbosacral disk space had practically no localizing significance. Myelography was considered the most reliable method of determining the level (accuracy of 79%). The operation consisted of exploration, with removal of the ruptured disk if such a condition was present. Fusion was performed in only 3% of the cases. When the exploration remained negative, chordotomy, rhizotomy, and spinal fusion were considered inadvisable.

The over-all surgical results were good: In the group of ruptured disks, 25% of the patients stated that they were "cured" and 67% improved (a total of 92% improvement). Among the negative explorations, 14% were cured and 74% improved (a total of 88%). The results in patients with bulging posterior ligaments were equally as good as those with truly ruptured disks and free fragments. Even though 12% of the disk patients and 23% of the patients with negative explorations wore back braces postoperatively, none of them required a subsequent fusion operation.

LIST, Grand Rapids, Mich.

PAPILLEDEMA AND PSEUDOTUMOR CEREBRI FOLLOWING POLIOMYELITIS. H. H. GASS, A. M. A. J. Dis. Child. 93:640 (June) 1957.

Gass reports on two children who, approximately two months after an attack of poliomyelitis, developed headache, vomiting, double vision, and severe papilledema. Ventriculography revealed a normal condition in both; the fluid removed during these procedures contained 15 and 6 mg. of protein per 100 cc., respectively, and 3 leukocytes per cubic millimeter in one. Subtemporal decompression was carried out in both cases, with prompt subsidence of the symptoms and of the papilledema within several weeks; the decompression site was flat within about six months.

The actual pathogenesis of this condition is unknown.

SIEKERT, Rochester, Minn.

DIAGNOSIS, TREATMENT, AND PROGNOSIS OF TUMORS AFFECTING THE SPINAL CORD IN CHILDREN. F. C. GRANT and G. M. AUSTIN, J. Neurosurg. 13:535 (Nov.) 1956.

Tumors of the spinal cord in children are relatively infrequent. In the authors' series of 409 spinal cord tumors, only 30 were found in children under 15 years of age. Metastatic tumors or seeded tumors from cerebellar medulloblastomas were not included. The onset was obscure and of extremely short duration because of their progressive growth and the frequent history of trauma.

Thirteen children were completely paraplegic at the time of surgery, nine having a flaccid type and four being of the spastic type. Only one who showed a flaccid paraplegia recovered. The authors emphasize the importance of early recognition of spinal cord tumors in children, for the prognosis of recovery from paraplegias due to extradural tumors is better in children than in adults. The commonest complaint was back pain, and the predominant neurologic sign was a sensory level to pinprick. Sixty per cent of the tumors were benign, the mortality rate being only 6.7%.

MANDEL, Philadelphia.

SPONTANEOUS HEMATOMYELIA AND ANGIOMAS OF THE SPINAL CORD. G. L. ODOM, B. WOODHALL, and G. MARGOLIS. J. Neurosurg. 14:192 (March) 1957.

Spontaneous hematomyelia has been used to describe the sudden onset of pain and rapid development of long-tract signs in a previously asymptomatic patient. The etiology has been obscure in many of the previously reported cases, although syphilis, trauma, myelitis, and tumor have been listed as isolated causes.

The authors report three cases of spontaneous hematomyelia secondary to intramedullary angiomas and three cases of extramedullary venous or arteriovenous angiomas. In the first group of cases there was a sudden onset of severe pain, followed by the rapid development of long-tract signs. In the extramedullary angiomas root pain was a prominent feature, with the gradual development of long-tract signs.

The intramedullary angiomas were found in the posterior columns of the cord without involvement of the pial vessels. Bleeding was confined to the cord except in one case, where bleeding extended into the subarachnoid space. Early recognition is essential, for the clot which is limited to the posterior columns can be more easily evacuated by surgery.

The extramedullary angiomas were found in the cervical and thoracic regions, and were accompanied by profuse subarachnoid hemorrhage. The myelogram revealed a tortuous serpentine defect over the involved segments of the cord. Surgery has little to offer in cases of extramedullary angiomas. Roentgen-ray therapy does not alter their course.

MANDEL, Philadelphia.

SPINAL CORD INVOLVEMENT IN MULTIPLE MYELOMATOSIS. E. CLARKE, Brain 79:332, 1956.

Clarke reports a series of 20 cases of multiple myeloma with spinal cord involvement. Spinal compression was found in 20% of the cases resulting from extension of the tumor from the vertebra, with or without bony collapse, or from a primary extradural myeloma. Most of the cases occurred in the thoracic region where the vertebral body or bony lamina was invaded. The dura mater was not involved usually, and in the microscopic examination it appeared to resist the infiltration of the myelomatous tissue. In this series, there were four cases of extradural compression without bony involvement.

Pain was the commonest symptom, aggravation being produced by root compression. Local tenderness and pain upon movement were present in most of the cases. The treatment of choice consisted of surgical removal, followed by irradiation.

MANDEL, Philadelphia.

ABSTRACTS FROM CURRENT LITERATURE

RADIOACTIVE VITAMIN B₁₂ IN DIAGNOSIS OF NEUROLOGICAL DISORDERS. G. M. BERLYNE, L. A. LIVERSEGE, and E. W. EMERY, *Lancet* 1:294 (Feb. 9) 1957.

The authors publish their results and technique in the utilization of radioactive cyanocobalamin (vitamin B₁₂) in the diagnosis of uncertain cases of subacute combined degeneration of the spinal cord. Results of an excretion test with radioactive cyanocobalamin, which they describe, lead them to conclude that this test confirms or excludes the diagnosis with reasonable certainty. The test depends on demonstrating incapacity to absorb cyanocobalamin. They utilized cyanocobalamin labeled with Co⁶⁰. They point out that investigation of the myeloneuropathies is often complicated by the fact that patients have received injections of liver or cyanocobalamin, when marrow examination and serum-vitamin B₁₂ levels are misleading, but the excretion test remains unaffected. Thus, in doubtful cases treatment with cyanocobalamin may be begun before the excretion test.

YASKIN, Camden, N. J.

LOCAL NEUROLOGICAL DISTURBANCES AND CHANGES IN THE OPTIC NERVE IN ANGIONEUROTIC DISORDERS (QUINCKE'S DISEASE). B. S. VILENSKII, *Zhur. Nevropat i psikiat.* 56:536, 1956.

The findings on clinical and ophthalmological investigation of two cases of Quincke's disease are reported. The first of the cases was marked by the sudden onset of left ophthalmoplegia, loss of vision in the right eye, right hemiparesis, and speech disturbances, occurring in close connection with the appearance of numerous swellings covering the entire left half of the face. The local neurological manifestations described never appeared except with Quincke's disease, and each time they disappeared rapidly *pari passu* with the disappearance of the facial swellings. It is to be inferred that in this patient the vessels of neurovascular disturbances involved not only the region of the face but also the vessels of the leptomeninges, and evidently also the vessels supplying the optic nerve and the eyeball. In the second case, a connection was noted between the progressive loss of vision in one eye and a succession of large swellings of acute onset on one side of the face—here, evidently, anterior cranial fossa and the right orbit. According to the literature and the author's data, the loss of the motor and speech functions occurring at the same time as widespread angioneurotic swellings is less marked, less prolonged, and less persistent than the changes in the optic and oculomotor nerves. Pareses and aphasic disturbances disappear completely after some hours, whereas the changes in the ocular fundus, diminution of visual acuity, and oculomotor disturbances are observed for as long as 24 hours after the disappearance of the acute swelling. So extensive can be the changes in the optic nerves following repeated neurovascular attacks that they may lead to atrophy of the optic nerve fibers and to a marked deterioration in vision which cannot be corrected. This can possibly be explained by the peculiar property of the optic nerve fibers of being highly vulnerable to vascular disturbances, and also by the peculiarities of the blood supply to the optic nerves (absence of collaterals).

BABENKOVA, Moscow.

Peripheral and Cranial Nerves

SHOULDER-HAND SYNDROME FOLLOWING MYOCARDIAL INFARCTION WITH SPECIAL REFERENCE TO PROGNOSIS. J. EDEIKEN, *Circulation* 16:14 (July) 1957.

Edeiken studied 42 patients who suffered 47 attacks of myocardial infarction, 43 of which were followed by the shoulder-hand syndrome. The earliest onset of the painful hand and shoulder occurred two weeks after the myocardial infarct, and in the majority of cases the onset was within four months. Twenty-nine patients obtained complete relief within 8 months after the onset of the shoulder-hand syndrome; nine patients recovered after 10 to 17 months; in one the duration was 22 months, and in two the pain lasted 2 years. Two patients were without relief for 27 and 36 months, respectively, at the time of the report.

The syndrome was not always complete, involving only the shoulder or only the hand in some patients, while in others both sides were affected. No correlation could be established with the severity, the extent, or the location of the myocardial lesion.

None of the 42 patients received any treatment except heat, analgesics, and exercise of the affected extremities.

The author has made it a practice to instruct all patients with coronary occlusion to move their arms and shoulders while in bed and to rest their heads on their hands 15-20 minutes three or four times daily. Since the establishment of this regimen, the severe types of shoulder-hand syndrome have been seen only infrequently.

FOLEY, Boston.

Treatment, Neurosurgery

PNEUMOCOCCAL ENDOCARDITIS, MENINGITIS, AND RUPTURE OF THE AORTIC VALVE. R. AUSTRIAN, A. M. A. Arch. Int. Med. 99:539 (April) 1957.

Austrian reports the results of penicillin treatment in eight patients over 40 years of age with pneumococcal endocarditis. The bacterial activity causing pneumonitis, endocarditis, and frequently associated pneumococcal meningitis was successfully arrested by penicillin, but the changes in the aortic valve produced marked insufficiency and perforation or rupture of the valve, with resultant cardiac failure and fatal issue in three-quarters of the cases. The author notes, but does not explain, the frequency with which meningitis complicates pneumococcal endocarditis, an association which was noted by Osler in connection with endocarditis, as well as with inflammation implicating the apices of the lungs. It would appear that about 25% to 30% of cases of pneumococcal meningitis present the triad referred to, and the presence of an aortic diastolic murmur with or without signs of cardiac failure in a patient with meningitis should suggest the pneumococcal nature of the infection.

PARSONS, Montrose, N. Y.

HEPATOLENTICULAR DEGENERATION. G. S. FERRISS and S. BERRY, A. M. A. Arch. Int. Med. 99:656 (April) 1957.

Ferriss and Berry make a follow-up report on a 32-year-old man with a two-and-a-half year history of Wilson's disease, treated with temporary physical and psychiatric benefit with dimercaprol. He was then lost sight of over the next two years. At the end of this two-year period chelation therapy with dimercaprol (BAL) was resumed, and supplemented by oral potassium sulfide (to bind the copper and prevent alimentary absorption) and high-protein diet (to promote urinary excretion of copper). Within five days improvement was noted; unassisted ambulation was possible within two months, and most of the routine acts of daily living were satisfactorily executed without assistance by the end of three months, after which little further change occurred during the final two months prior to discharge, despite continuance of therapy. The spinal fluid protein, which had been 106 mg. per 100 cc. prior to treatment, had fallen to 73 mg. per 100 cc. upon discharge. It is stated that the patient continued to be uninhibitedly exhibitionistic, showing sexual preoccupation and expressions "intolerable to personnel." Unfortunately, little indication of additional observations concerning the status of intellectual functions, especially with respect to memory, orientation, calculation, reasoning, abstractions, and judgment, is supplied. The early use of the rapid and simple test for serum oxidase activity in instances in which this disease is suspected is advocated, as some evidence of superior therapeutic results with prompt and early treatment is available.

PARSONS, Montrose, N. Y.

ANTIEMETIC PROPERTIES OF A NEW CHLORPHENOTHIAZINE DERIVATIVE, PROCLORPERAZINE. D. G. FRIEND and G. A. McLEMORE, A. M. A. Arch. Int. Med. 99:732 (May) 1957.

Prochlorperazine, a substance combining the structural characteristics of both the piperazine and the phenothiazine series of drugs, was utilized for presumed antiemetic effect in the treatment of 25 cases of nausea and vomiting of various causes, including two of Ménière's syndrome. It was found to be more effective than chlorpromazine and to be effective at approximately half the usual dose required in the case of the latter medicament. This factor of lower dosage with greater antiemetic affect results in less toxicity than is encountered with chlorpromazine. Prochlorperazine was additionally noted to show about half the hypotensive and sympathetic depressant action of chlorpromazine. No hepatic or hematologic alterations developed during therapy. The absence of significant toxic side-reactions plus the superior antiemetic action suggests the suitability of the use of prochlorperazine in controlling intractable vomiting seen in gastric crises, hypertensive encephalopathy, Ménière's disease, etc.

PARSONS, Montrose, N. Y.

ABSTRACTS FROM CURRENT LITERATURE

METHARBITAL (GEMONIL) IN MYOCLONIC SPASMS OF INFANCY AND RELATED DISORDERS.

M. A. PERLSTEIN, A. M. A. J. Dis. Child. 93:425 (April) 1957.

On the basis of 200 patients of all ages with 248 clinical entities, Perlstein concludes that metharbital is (1) practically nontoxic; (2) effective in seizures associated with organic brain disease (41%) as compared with "idiopathic forms" (6%); (3) most effective in myoclonic spasms of infancy (66%), defined as sudden, momentary, generalized spasms, principally of the limbs, and (4) occasionally of benefit in focal and generalized seizures. The dosage varied from 15 to 180 mg. two to four times a day.

SIEKERT, Rochester, Minn.

CRYPTOCOCCUS MENINGITIS ARRESTED WITH AMPHOTERICIN. B. E. APPELBAUM and S. SHTOKALKO, Ann. Int. Med. 47:346 (Aug.) 1957.

The case of a 46-year-old white woman with the diagnosis of cryptococcal meningitis established by spinal fluid studies and mouse inoculations is reported. Within two weeks following the institution of parenteral therapy with Amphotericin B (100 mg. once daily for 12 days in dextrose and subsequently once every second day for 5 weeks), evidence of clinical improvement was noted, particularly in clearing of the sensorium. At the time of writing, eight months later, no neurologic residues were present.

AIGNER, Rochester, Minn.

TREATMENT OF PROGRESSIVE MUSCULAR DYSTROPHY WITH ADENOSINETRIPHOSPHORIC ACID.

B. P. MANKOVSKI and V. M. SLNIMSKAYA, Zhur. nevropat. i psikhiat. 55:43, 1955.

The treatment of progressive muscular dystrophy with adenosinetriphosphoric acid was studied in 150 patients, of whom 110 had progressive muscular dystrophy and 40 had other neurological diseases (polyneuritis, poliomyelitis, myasthenia), the diseases having existed from 1 to 20 years. Most of the patients received three to five courses of treatment, a course consisting of 40 intramuscular injections of the monocalcium salt of adenosinetriphosphoric acid (30 mg. in 1 ml. of isotonic saline per injection). No side-effects were seen with this preparation. Of the 110 patients with progressive muscular dystrophy, 100 responded favorably, the muscular atrophy improving and the range of movements and muscular strength increasing. In most instances the tendon reflexes reappeared. The muscular reaction to electrical stimulation increased, chronaxy became practically normal, and creatine metabolism improved. The therapeutic effects are ascribed to the favorable influence of the preparation, via the nervous system, on the metabolism of substances in the muscular tissue.

GOLLAND, Moscow.

Muscular System

MYASTHENIA GRAVIS DEVELOPING FIFTEEN MONTHS AFTER REMOVAL OF THYMOMA. M. J.

MADONICK, M. RUBIN, L. H. LEVINE, and W. KARLINER, A. M. A. Arch. Int. Med. 99:151 (Jan.) 1957.

The authors add another case to the four previously described in the literature wherein myasthenia gravis has appeared after removal of a thymoma. A 33-year-old Negro woman developed myasthenic symptoms 15 months after removal of a benign thymoma. A favorable response to neostigmine therapy was initially obtained. Over a period of approximately six months there was progressive increase in the severity of the myasthenic symptoms. The thorax was reexplored, despite lack of x-ray evidence suggesting a thymic mass, and a mass of normal thymic was removed, with improvement, although continued neostigmine therapy was necessary. The authors indicate the necessity of surgical exploration for the presence of thymic lesions in the face of severe progressive, medically refractory myasthenia gravis, despite lack of roentgenologic evidence of a thymic lesion; on the other hand, it is stressed that the relationship between the presence of myasthenic symptoms and thymic pathology is obscure.

PARSONS, Montrose, N. Y.

RARE VARIANT OF MYOTONIA ATROPHICA—CLINICAL AND ELECTROMYOGRAPHIC STUDY OF A FAMILY. D. K. ZIEGLER and J. ROGOFF, Brain 79:349, 1956.

The syndrome of myotonia atrophica consists of myotonia, muscular atrophy, lenticular cataract, and premature baldness, with testicular atrophy in the male. The condition is

strongly familial, although the exact genetic manner of inheritance is unknown. Ziegler and Rogoff report a family in which all of the manifestations of myotonia atrophica except myotonia were seen in varying degrees in different members of two generations. Clinical myotonia was seen only in one patient after exposure of the hands to ice water. The electromyographic pattern was typical in these cases, the high-frequency rhythmic spikes giving the characteristic "dive-bomber" myotonia potential. An unusual neurological syndrome also occurred in the family, characterized by peripheral sensory loss, pes cavus, scoliosis, mental deficiency, and fasciculations, in one case. There was some difficulty in determining whether the fasciculations were myogenic or neurogenic from the electromyogram in this case.

MANDEL, Philadelphia

A NEW CONGENITAL NON-PROGRESSIVE MYOPATHY. M. G. SHY and K. R. MAGEE, *Brain* 79:610, 1956.

Shy and Magee report five cases in three generations of the same family of a non-progressive myopathy with a characteristic pathognomonic alteration of the muscle fiber. The patients in this series ranged from 2 to 65 years of age, and the pattern of inheritance suggested a Mendelian dominant without sex linkage. Clinically, each case was characterized by delayed motor development and bizarre posturing. One child could not turn in bed until 10 months of age, and all were delayed in walking until the age of 4 or 5 years. All complained of difficulty in climbing stairs, running, or rising from the supine or sitting position. The adults gave a history of minimal weakness in the upper extremities, occurring during vigorous activities. There were no sensory or cranial nerve symptoms.

Neurological examination revealed primarily proximal weakness, which was severest in the lower extremities. Some cases exhibited distal weakness as well. All patients were ambulatory and were able to perform useful duties. Hypotonia was present only in the children, and wasting was not a prominent feature. No myotonia could be demonstrated clinically or electromyographically. The deep tendon reflexes were normal.

The principal pathologic feature of the muscles subjected to biopsy from these cases was the anatomical arrangement of aberrant fibrillary bundles found in the center of each muscle fiber. These fibers gave a more positive periodic acid-Schiff reaction than did the peripheral fibrils and, in addition, were more argentophilic than the peripheral fibers.

MANDEL, Philadelphia

Encephalography, Ventriculography and Roentgenography

MYELOGRAPHIC DEMONSTRATION OF BRACHIAL PLEXUS ROOT AVULSION. R. A. MENDELSON, I. H. WEINER, and J. M. KEEGAN, *A. M. A. Arch. Surg.* 75:102 (July) 1957.

Myelography frequently demonstrates nerve root avulsion in cases of stretch injury of the brachial plexus (in 7 out of 11 cases in the authors' material). The characteristic roentgenologic appearance of root avulsion is that of bulbous extradural outpouchings extending into the extravertebral space. This finding presumably indicates the presence of a traumatic meningocele at the site of the torn root. The roentgenologic changes, however, do not always correspond to the clinical level of the lesion. Myelography proved a useful adjunct in diagnosis. It permits accurate prognostication and management of brachial plexus injuries. If a nerve root avulsion can be shown, exploration of the brachial plexus is not indicated but reconstructive surgery should be done early.

LIST, Grand Rapids, Mich.

CORRELATION OF PAIN AND THE ROENTGENOGRAPHIC FINDINGS OF SPONDYLOSIS OF THE CERVICAL AND LUMBAR SPINE. A. E. HUSSAR and E. J. GULLEE, *Am. J. M. Sc.* 232:518 (Nov.) 1956.

Five hundred male employees, ranging in age from 18 to 65 years, had roentgenographic examinations of the cervical and lumbar spine for assessment of the clinical significance of spondylosis. The films were examined for the presence of bony spurs, narrowing of the disk spaces, and abnormalities of the apophyseal joints. Of the 500 subjects, 38 complained of cervical pain, and 84 showed evidence of spondylotic changes. Lumbar pain was complained of by 95 subjects, and 115 showed findings of spondylosis. Statistical analysis revealed a low correlation between the incidence of pain and positive roentgenographic findings but a

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high correlation between age and findings of spondylosis. It was concluded that the roentgenograms are of dubious value in diagnoses of encroachment in the nerves by spondylitic changes.
BERLIN, New York.

THE SIGNIFICANCE OF THINNING OF THE PARIETAL BONES. H. L. STEINBACH and W. G. OBATA, *Am. J. Roentgenol.* 78:39 (July) 1957.

Thinning of the parietal bones has frequently been described by roentgenologists. The lesion was observed by pathologists before the x-ray was discovered. The lesion appears in a roentgenogram as a depression of the outer contour of a portion of the parietal bone. The calvaria is thin in the area of involvement, primarily as the result of a decrease in thickness of the diploe. The outer table of the skull retains its normal thickness unless the lesion is severe. The thinning is almost always bilateral, although some cases of unilateral involvement have been reported.

Some observers have felt that parietal thinning is a static process, rather than a progressive one, and for this reason have preferred to call it "parietal thinness." Steinbach and Obata report a case of parietal thinning in which serial roentgenograms show definite progression of the process. The patient was an 85-year-old woman who had had a reticulum-cell sarcoma of the stomach removed 17 years previously. Serial roentgenograms of the skull were available from 1937 to 1955. In the original films only a very slight symmetrical thinning of the parietal bones could be appreciated. The finding was actually on the borderline of normal. Films made in 1953 showed a marked thinning of the parietal bones, so that only a thin shell, representing the inner table of the bones, remained in the involved area. In 1955 the skull appeared about the same as it had appeared in 1953. Films of other bones in the body showed only a generalized osteoporosis. It is thought that thinning of the parietal bones is often associated with generalized osteoporosis. Steinbach and Obata also report two additional cases of parietal thinning which occurred in younger male patients with gonadal insufficiency.

The cause of parietal thinning and the mechanism of its occurrence are not known. Steinbach and Obata point out that the thinning occurs in the only part of the calvaria that is not the site of muscular attachment. The portion of the parietal bone in which thinning occurs is covered by the galea aponeurotica, which has no connection to the parietal bone and actually moves a considerable distance over it as a result of contraction or relaxation of the adjacent musculature. It thus might be possible to explain the localized thinning of the parietal bone on the basis of decreased osteoblastic activity as a result of gonadal insufficiency, senility, or other causes of osteoporosis. In the external parietal region there is little stress or strain to stimulate an opposing increase in activity, whereas pressure of the brain internally and of the muscles externally produce some stress and strain on the rest of the skull.

WEILAND, Grove City, Pa.

ROENTGENOGRAPHIC DIAGNOSIS OF SPINAL TUMORS. A. S. TUCKER, B. ARAMSRI, and C. R. HUGHES, *Am. J. Roentgenol.* 78:54 (July) 1957.

The authors review 96 neoplasms of the spine diagnosed at the Cleveland Clinic from 1949 to 1955. They add their results to a series from the same institution covering the period before 1949, and previously published. The total of all neoplasms of the spine in both series is 167. Of these tumors, 34% were neurofibromas, 28% meningiomas, 9% gliomas, and 9% ependymomas. The other 20% were made up of nine different types of tumors. Twenty-three of 32 extradural tumors in the authors' series could be diagnosed by the plain roentgenograms of the spine. Of these 32 extradural tumors, 22 could be diagnosed by myelograms. Only 9 of 53 intradural tumors could be diagnosed by the plain roentgenograms of the spine, but 47 of them could be diagnosed by myelograms. None of the 11 intramedullary tumors were diagnosed by the plain roentgenograms of the spine, but 7 of them were diagnosed by myelograms.

It is important to make good-quality roentgenograms of the spine in all patients suspected of having a spinal cord tumor. These roentgenograms must be studied carefully for any evidence of erosion or infiltration of the bone. Oblique views and laminagrams are helpful in visualizing a suspected abnormal area a little better. When roentgenograms fail to reveal an abnormality but the symptoms or signs suggest a lesion of the spine, myelography is indicated. Myelograms helped in making the proper diagnosis in 76 of the 96 cases described here.

WEILAND, Grove City, Pa.

THE VERTEBRAL VEIN SYSTEM. O. V. BATSON, Am. J. Roentgenol. 78:195 (Aug.) 1957.

Batson presents a scholarly discussion of the history of our anatomical knowledge of the vertebral veins. Although anatomists have been aware of the presence of the vertebral veins for centuries, there is little evidence that they have appreciated the extensiveness of the vertebral vein system and its relation to the other major venous systems of the body. Breschet worked in the early part of the 19th century and achieved a rather thorough knowledge of the vertebral vein system for that time. He left large, precise, and well-done illustrations, which are among the best we have today, although they are poorly known.

Batson has studied the vertebral vein system extensively by injection techniques, obtaining corrosion specimens and roentgenograms after the injection of radiopaque material. In studying the intrapelvic communications of the vertebral veins in regard to the possible spread of carcinoma of the prostate, Batson elected to enter the prostatic plexus of veins by injection through the deep dorsal vein of the penis. Injection was performed on a cadaver lying in the dorsal recumbent position. Since the vena cava is at a higher hydrostatic level in this position, most of the material remained in the spinal veins. By increasing the amount of injection, the material spread as far as the cranial veins. The parallelism between the architecture of the injected venous network and the pattern of distribution of prostatic metastases was striking.

Batson views the veins of the human body as being composed of two principal groups: (1) those within the pressure chamber of the thoracoabdominal cavity, and (2) those outside this cavity. The first group of veins, within the cavity, consists of the caval, the pulmonary, the portal, and the lumboazygos veins. The veins of the extremities which possess valves are a part of the caval system. The second group of veins, those outside the cavity, Batson calls the vertebral vein system. It consists of veins of the head and neck, the veins of the body wall, and the valveless veins of the extremities. All of these vessels are continuous with the veins of the vertebral column. The vertebral system parallels, joins, and also bypasses the cavity veins. It unites the superior vena cava with the inferior vena cava, as the azygos veins do, but the union provided by the vertebral vein system lies outside the pressure cavity of the body. A close communication is provided between the vertebral vein system and the bone marrow by the large emissary veins in the bodies of the vertebrae. The vertebral vein system is valveless. The flow of blood in the system can be reversed in different sections in response to pressure changes in the cavity system. Knowledge of the existence of this large valveless vertebral system, which by-passes the caval system, illuminates the problems of routes of various metastases and of collateral circulation in venous thrombosis.

WEILAND, Grove City, Pa.

METASTATIC RETINOBLASTOMA AS A CAUSE OF DIFFUSE INTRACRANIAL CALCIFICATION. L. A. DAVIS and I. DIAMOND, Am. J. Roentgenol. 78:437 (Sept.) 1957.

Calcification in retinoblastomas has been identified in roentgenograms in as high as 75% of cases. However, it is almost always limited to the region of the orbit. Often it is demonstrated only after roentgenographic examination of the operative specimen. Davis and Diamond report the case of an infant having unilocular retinoblastoma extending into the middle cerebral fossa and producing hydrocephalus. The tumor also produced extensive visceral metastases. The skull roentgenograms showed extensive punctate intracerebral calcifications in the region of the basal ganglia on the left side. Autopsy revealed gross calcifications in the primary tumor in the eye, and a large metastatic mass was found in the subarachnoid space, occupying the interpeduncular fossa and invading the brain and pituitary gland. This mass contained gross calcification.

WEILAND, Grove City, Pa.

EOSINOPHILIC GRANULOMA OF BONE. L. G. TEPLICK and H. BRODER, Am. J. Roentgenol. 78:502 (Sept.) 1957.

Teplick and Broder report an atypical case of eosinophilic granuloma which occurred in an elderly woman and discuss the general problem of eosinophilic granuloma and the relationship of the tumor to Hand-Schüller-Christian disease and to Letterer-Siwe disease.

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By serial roentgenologic examination, Teplick and Broder were able to observe an eosinophilic granuloma develop. The first films revealed simply some radiolucent areas in the acromion process and an irregular linear plaque of calcification in the adjacent soft tissues. A little more than a month later a second set of films were exposed and revealed extensive, irregular destruction of the edge of the acromion process and the distal end of the clavicle. After the second set of roentgenograms, the diagnosis of the eosinophilic granuloma was made by the hospital pathologist by means of biopsy. Confirmation by a number of other pathologists was sought and obtained because of the unusual nature of the tumor. It is unusual for a patient of this age to develop eosinophilic granuloma; the tumor progressed unusually rapidly; it apparently crossed a joint, which is unusual for this or any other primary bone tumor, and the tumor began primarily as a soft-tissue tumor, so far as could be observed in the roentgenograms. The clinical history and the microscopic findings were considered typical for eosinophilic granuloma despite the conflicting roentgenographic evidence. The lesion responded exceptionally well to deep x-ray therapy, did not recur within a year, and no similar lesions were found elsewhere in the skeleton.

WEILAND, Grove City, Pa.

CEREBRAL ANGIOGRAPHY IN ENCEPHALO-TRIGEMINAL ANGIOMATOSIS. C. M. POSER and J. M. TAVERAS, *Radiology* 68:327 (March) 1957.

Poser and Taveras have collected a series of 15 cases of encephalotrigeminal angiomas in which they have performed a cerebral angiogram on each patient. They divided their 15 patients into three clinical categories: (1) typical Struge-Weber encephalotrigeminal angiomas, in which a port-wine nevus is present on the skin of the face and there are symptoms of abnormality within the central nervous system, such as convulsions, hemiparesis, mental retardation, etc.; (2) the incomplete form in which skin lesions are absent but the other classical features of the syndrome are present; (3) atypical cases, in which some type of vascular anomaly of the skin of the face other than the port-wine nevus is present along with some other feature of the syndrome.

Poser and Taveras then selected 35 cases from the medical literature in which this syndrome had also been described and in which cerebral angiograms had been performed. Combination of these 35 cases with their own 15 cases allowed them to evaluate a series of 50 cases. Of these 50 cases, the cerebral angiogram revealed some abnormality of the cerebral vascular system in 23. In addition to the classical capillary-venous angioma which has usually been described in this syndrome, other anomalies were found: arteriovenous malformations, arterial thromboses, anomalies of veins and the dural sinuses, subdural hematomas, and cerebral atrophy or hypoplasia. Intracranial calcification was visible on the plain skull roentgenograms in 27 of 47 cases. Abnormal findings in the cerebral angiogram occurred only in 10 of the 27 cases showing calcification, but 13 of the 20 cases without calcification had abnormal angiograms. Two patients in whom vascular anomalies were demonstrated but no calcification showed in the plain films of the skull were followed by serial roentgenograms. It was found in these two patients that a rather massive Weber-type calcification developed rapidly. Poser and Taveras draw the conclusion that if an intracranial angioma can be shown by cerebral angiography, rapid and massive cortical calcification probably will develop.

WEILAND, Grove City, Pa.

ANGIOGRAPHIC DEMONSTRATION OF THE PRIMITIVE TRIGEMINAL ARTERY. B. L. WISE, *Radiology* 68:731 (May) 1957.

Wise reports the case of a 29-year-old white woman in whose cerebral angiogram a carotid-basilar anastomosis was demonstrated. This is a rare congenital cerebral vascular anomaly, which is thought to result from failure of regression of the primitive fetal trigeminal arteries. In this patient a right carotid angiogram showed a large vascular channel joining the proximal subclinoid portion of the internal carotid artery with the midportion of the basilar artery. The portion of the basilar artery distal to this channel and both posterior cerebral arteries were well filled with the opaque medium.

The patient was studied because she had begun to have episodes of automatic behavior and amnesia and episodes of rage. She was a heavy drinker. The electroencephalogram made with the patient awake was normal. The electroencephalogram made during sleeping showed slowing

and sharp waves in the right parietal and occipital areas. The congenital vascular abnormality was not thought likely to be related to the patient's symptoms.

WEILAND, Grove City, Pa.

TRIGONOCEPHALY. P. A. RIEMENSCHNEIDER, *Radiology* 68:863 (June) 1957.

Trigonocephaly is a congenital deformity of the skull characterized by a keel-like ridge at the site of the metopic suture. Riemenschneider presents skull films of two patients showing this deformity. In both patients, the frontal bone was small; the orbits were set closely together, and the anterior cranial fossa was shallow. The metopic suture was closed in one patient and open in the other. Some authors have hypothesized that the deformity is caused by premature closure of the metopic suture in the fetus. Riemenschneider believes that the deformity has nothing to do with premature closure of any suture but that the underlying deficiency is a hypoplasia of the frontal lobes of the brain. As a result of this hypoplasia there is poor development of the ethmoid and frontal bones, leading to the deformity which has been described.

WEILAND, Grove City, Pa.

RAPID OSSEOUS CHANGES IN SYRINGOMYELIA. G. A. MYER, J. STEIN, and M. H. POPPEL, *Radiology* 69:415 (Sept.) 1957.

Ninety per cent of neuropathic arthropathies are associated with tabes dorsalis, while the remaining 10% are caused predominantly by syringomyelia. It has been assumed that the lesions of the nervous system produce areas of analgesia in the affected joint and that repeated trauma occurs from ordinary motion of the joint when analgesia is present. Neuropathic arthropathies are found more frequently in the joints of the lower extremity and usually progress more rapidly in these joints because weight-bearing is thought to provide the trauma required to produce the changes. This theory has been questioned by some authors because the affected joints are painful in a considerable number of the cases of syringomyelia and because joint destruction has been known to develop rapidly without any known trauma.

Myers, Stein, and Poppel report the case of a man, aged 37, who complained of numbness of the right upper extremity for four months. The numbness extended to the right side of the neck, the right occipital area, and behind the right ear. He was found to have hypesthesia, hypalgesia, and diminished temperature sensation in the area supplied by the dermatomes C-2 through C-8. He had no demonstrable muscle reflexes in the right arm. The right deltoid and biceps muscles were weak, and there was some atrophy of the biceps muscle. Roentgenograms of the right shoulder demonstrated erosive changes involving the greater tuberosity of the humerus and the distal end of the acromion process. About two months later he developed pain in the right shoulder, which was sharp and became progressively severer. A second set of roentgenograms was exposed about 10 weeks after the original set. The second set showed absorption of the major portion of the head and neck of the right humerus. Roentgenograms made about five months after the original ones showed extensive soft-tissue calcification and periosteal proliferation along the upper end of the humerus. The remaining portion of the humerus showed subluxation in relation to the glenoid fossa. The diagnosis made was syringomyelia with a neurotrophic joint. The case is presented because it illustrates extremely rapid destructive changes in a neurotrophic joint which does not bear weight.

WEILAND, Grove City, Pa.

TECHNICAL AND DIAGNOSTIC PROBLEMS OF PNEUMOENCEPHALOGRAPHY AND VENTRICULOGRAPHY IN TUMORS OF THE POSTERIOR FOSSA. G. CASTORINA and P. SEVERINI, *Fortschr. Geb. Röntgenstrahlen* 86:216 (Feb.) 1957.

Castorina and Severini discuss a series of 35 cases of verified posterior fossa tumors in which pneumoencephalography was used and 26 cases in which ventriculography was employed. The combined method resulted in adequate ventricular filling in 58% of cases; only 43% of those accorded pneumoencephalography alone had adequate visualization of fluid pathways. The authors stress the advantages of the combined method from the standpoint of its comparative safety in posterior-fossa-tumor suspects, and its permitting of satisfactory visualization of aqueduct, fourth ventricle, and cisterns, making possible the differentiation of clivus and pontine intra- and extramedullary midline tumors from one another, as well as from lateral cerebello-pontine-angle lesions.

PARSONS, Montrose, N. Y.



SECTION ON PSYCHIATRY

Psychotherapy in a Home for the Aged

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Introduction

The psychiatrist who undertakes the treatment of emotional disorders in a home for the aged is early impressed with the need to explore his own attitudes, prejudices, and misconceptions about old people.

As a member of a culture which extols youth, competitiveness, attractiveness, and success, he must face up to the degree with which he is tainted with social attitudes of distaste for the old. In particular need of perusal is the degree of uncritical acceptance by the therapist of widely believed generalizations and stereotypes about the personalities of the aged. Among these are notions that the old are rigid, conservative, inattentive, garrulous, difficult to educate, and subject to anacletic or narcissistic object relations. In spite of convincing evidence to the contrary,¹⁰ the notion is still widespread that disorganized and confused states in senescent patients are caused by irreversible senile and arteriosclerotic changes in the brain.

In psychodynamic formulations about their neuroses, there may be a tendency to overemphasize adaptive utilization of dependency techniques in response to the many

real deprivations in the environment and in the physical health. This overemphasis of one operational concept may lead to the neglect or elimination of another useful concept. This concept views old people's anxiety as partly in reaction to the threat that an ego, whose repressive forces are weakened by the traumas of aging, may now be overwhelmed by previously warded off ego-alien drives. In preoccupation with the security needs of the aged, one may overlook their sexual problems. This can pose a double-edged problem in therapy. For the patient, in his own acceptance of social taboos on sex for the old, is much less disposed to bring up sexual matters than is the case with younger patients. Another problem may have to do with the therapist's attitude toward somatic complaints. In younger patients, one may have to guard against too ready an interpretation of somatic symptoms on a psychodynamic level. With the aged, there may be a tendency to accept a structural etiology too readily. For example, an old man's urinary frequency may express his urethral eroticism rather than prostatic enlargement. On the contrary, unsuspected organic pathology may be presented symbolically by old people in the form of emotional symptoms, as, for example, in the case reported by Goldfarb of an 88-year-old woman whose delusion that her eyeglasses had been stolen was the clue which led to the detection of acute glaucoma.⁴

Psychotherapy with aged patients may arouse specific anxieties in the therapist to a

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more disturbing degree than occurs in the treatment of younger people. For example, a provocative oldster may quickly stir up unresolved ambivalence toward one's own parents and grandparents. Also, when one's patients are near death and prone to a host of bodily ills, death and castration anxieties may be aroused in the therapist and pose serious countertransference problems.

Of the various prejudicial attitudes which the geriatric psychiatrists may have to overcome in himself, perhaps the most difficult is therapeutic pessimism, for at first sight, it appears warranted. His patients have few remaining years. Their neurotic adaptive patterns, brought with them into senescence, are masked by painfully real frustrations and loss of mates, friends, status, health, and usefulness. However, when a man has nothing, a little is a lot. It is a rare patient in a home for the aged for whom the psychiatrist cannot provide some palpable benefit, however small. It may be the pleasure of emotional ventilation to a sympathetic, uncritical listener, a new laxative or somnifacient, a change in diet or roommate, or renewed medical interest in an old physical complaint. But beyond this combined role of social worker and internist, the psychiatrist has a special function. This is based upon the observed propensity of our patients to display obvious parentifying behavior, in relation to authoritative persons in the Home. The therapist actively fosters this relationship and manipulates it to produce alterations in the patient's feeling and behavior. The attitude of therapeutic pessimism may undergo considerable change when one accepts the value of limited goals, and experiences how often they can be reached with these patients. As Rado cautioned, we do not aim to produce the best-adjusted people in the cemetery.⁹

Methods

The psychotherapy employed in the Home for Aged and Infirm Hebrews is empiric and eclectic. The various techniques blend one into another, but may be separated into

four types: (1) milieu therapy; (2) supportive and repressive therapy; (3) special supportive therapy, and (4) analytical psychotherapy. It should, of course, be emphasized that all of these techniques involve manipulation of transference. The differences are mainly in the methods of manipulation.

Milieu Therapy

By design, the Home is a therapeutic community. The psychiatrist functions as part of a team, which includes social workers, occupational therapists, physiotherapists, dietitians, physicians, and nurses. The psychiatrist attempts to enhance the therapeutic effect of the community by lectures and conferences with all members of the team. In these, he attempts to explain the patient's behavior and the rationale behind his specific recommendations. At the same time, in private conferences, he attempts to focus tactfully upon negative therapeutic attitudes on the part of staff members. The very presence of so many psychiatrists in the Home has a restraining effect upon unsavory staff behavior.

Supportive and Repressive Therapy

Many patients respond to such simple procedures as ventilation, reassurance, manipulations of environment, diet, and drugs. Only the psychiatrists are permitted to prescribe ataraxic drugs, providing a curb upon their indiscriminate use.

An 80-year-old woman asked for sleeping pills for severe insomnia. After several interviews it was learned that her insomnia began after her aged boy friend died in his sleep. After her unconscious fear of a similar fate was interpreted and discussed, her insomnia abated.

A 69-year-old man presented typically neurasthenic complaints. After several months he revealed that he masturbated regularly and had been warned by a physician that this would weaken him and damage his health. Reassurance resulted in marked improvement.

In occasional patients when other methods of treatment fail, repressive measures are used judiciously. This is based upon the well-known principle that when a culture

will not tolerate certain forms of behavior, these tend not to appear.

An 80-year-old woman presented a serious management problem because of a well-circumscribed delusion about mice. They tormented her by expelling flatus, screaming at night, and crawling on her bed. When other measures failed, she was told that she would have to become an infirmity patient and lose her room to protect her from the mice. The mouse delusion disappeared and was replaced by mild paranoid ideas about another woman.

A 72-year-old schizophrenic woman developed a catatonic episode in which she refused to speak or to take nourishment, and had to be tube-fed. She was told that she would be transferred to a State hospital if the tube feeding had to be continued. She resumed eating.

Special Supportive Therapy

As described in numerous papers by Goldfarb,²⁻⁵ this technique of treatment involves the ready acceptance by the therapist of the role which the patient projects upon him. Motivated in part by his loss of object relations and in part by the anxiety engendered by his helplessness and loss of mastery, the patient revives his techniques for dependency gratification. Thus, he casts the therapist in the role of a parent and attempts to ingratiate, coerce, or seduce him into providing the desired emotional gratification. The therapist is now in a position to identify the patient's transference wishes by following his associations and to fulfill them, whether they be for love and protection, or for reproaches and punishment. The patient is encouraged to leave a session with the illusion of having conquered the therapist, having borrowed or incorporated his omnipotence. This results in an increased feeling of worth and mastery, with subsequent diminution of anxiety.

An 84-year-old man carried a cane as a weapon, constantly demanded special treatment, and was known as an angry complainer during his four years in the Home. He was referred after he attempted to kill another resident. He was encouraged to formulate a picture of the therapist as a powerful person who could grant his requests, but would not because of his behavior. This had the desired effect of focalizing his rage onto the therapist, who, although slightly cowed, remained

friendly. He left his sessions victoriously, and his illusion of having conquered the therapist was cemented from time to time with real rewards for good behavior. He abandoned the cane and has not posed a management problem for the past three years.

Analytical Psychotherapy

This technique is employed with selected neurotic patients who are intelligent, have minimal organic mental impairment, and have the capacity to understand and utilize psychological concepts. With several exceptions, the technique resembles that used with young adults. The exceptions involve, first, the need to take into account the cultural setting of the Home, which is both unique and limiting. It encourages passive, submissive behavior with few opportunities for healthy self-assertion, as in the military. Second, the therapist must be much more supportive and directive than he would be with younger patients, and his formulations must be more intellectualized. Third, and perhaps most important, there is no indication for the resolution of the transference. The therapist is badly needed as a replacement for lost object relations. Not uncommonly, patients ask for direct reassurance that the relationship will continue until death, citing their half-hour a week as a *raison d'être*.

Results

Attempts to evaluate the results of psychotherapy with our patients are beset with the same difficulties that accompany similar evaluations in younger people. In those who improve, the question of whether the same results might not have been obtained without treatment can probably not be answered with scientific certainty. However, the therapist's conviction, based upon his intimate knowledge of the patient's mental life and behavior in treatment, may have more validity than independent ratings and statistics. One of the problems in our population concerns, on the one hand, how the patient feels, and, on the other, how the Home environment

feels about him. Happily, many of those who improve, improve by both standards. However, we have had depressed patients who achieved symptom remission in treatment, only to be considered problem residents by the administration because of their aggression being now directed against the environment.

Goldfarb and Turner studied the effectiveness of a brief-interview, supportive technique of therapy with our population.² The patients were rated in terms of their social adaptation. Of 41 cases of chronic brain syndrome with disordered behavior, 49% were found to be improved, 29% stabilized, and 22% unimproved. The average number of sessions was 8.5.

No statistical studies have been conducted for our other techniques of therapy. It is our experience, however, that a large proportion of our patients in treatment achieve appreciable gains. We hope that our findings will help to dispel the unwarranted pessimism that has limited psychotherapeutic efforts with old people.

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Measure of the Inadequacy in Schizophrenic Patients for Making Difficult Discriminative Evaluations

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Included in the many researches contrasting psychological processes of normally functioning and mentally disturbed persons are several which have been designed to study intraindividual variability. Several investigators of this problem—Gatewood²; Hunt³; Shakow and Huston⁷; Huston, Shakow, and Riggs,⁵ and Siegel⁸—are of the general opinion that increased intraindividual variability in psychomotor and mental tests is positively related to emotional disturbance. Stability in attitudes of young schizophrenic patients has been investigated by David and Rabinowitz,¹ who found these subjects to be less consistent than student nurses in expressing a preference. In their study, results were based on a test-retest situation. The present paper has the dual purpose of reporting further evidence for this finding, and of describing a procedure utilizing Paired Comparisons which provides an inconsistency score in a single testing session. In addition to the practical advantage of avoiding the need of seeing each patient a second time, any change in attitude which might occur as a result of experience during the time interval between testings is obviated. The inadequacy in schizophrenic patients for making difficult discriminative judgments has long been recognized but seldom measured. A quantification of this inadequacy, such as is provided by the techniques to be discussed, might be useful in making comparison of patients and of occasions of testing the same patient.

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Testing Procedures

Although the method employed is fundamentally that of Paired Comparisons, and the items have been scaled according to the traditional procedure, the primary aim of the study was to compare members of two groups on their ability to express consistent preferences regarding pairs of stimuli. Since the only task on the part of the subject is to make a choice between two items, the test is called the Choosing test.

Two forms of the test have been devised—Designs and Social Situations. For the former, the stimuli were 12 paper designs about 1½ in. square, each of one basic color and two contrasting colors. The designs were pasted by pairs on 4×6 in. cards, and, in order to permit comparisons among all stimuli, 66 cards were required. In addition, there was one practice card to acquaint the subject with the task, which was to state which of the two designs he preferred. Since all the forms were identical, color combination was the only basis for preference. The order was so arranged that on each six successive cards all 12 stimuli were presented, thus assuring a fairly equal representation of each design throughout the test.

The format for Social Situations was essentially the same as for Decisions; however, the stimuli were 12 statements describing undesirable social behavior. These were presented by pairs, and the subject was requested to select which of the two he considered worse. Whereas Designs involves an aesthetic judgment, Social Situations pertains to interpersonal relations and was expected to be a less pleasant task, especially for subjects who were victimized by strong feelings of guilt. Following are the 12 statements:

- A. For a person to play his television late at night, when he knows it disturbs his neighbors.
- B. For a girl to make a date with a man after hearing that he was already engaged.
- C. For a man to swear at a restaurant waitress because she made a mistake on his order.
- D. For a person to set back the speedometer on his car just before offering it for sale.
- E. For an employee to sneak inexpensive items away from his office and use them in his home.
- F. For a bride to serve a carelessly prepared meal to her husband's parents on their first visit.

- G. For a mother to spank her 2-year-old because he seems to be crying for nothing.
 H. For a young man to push past an elderly lady and take the last streetcar seat.
 I. For a wealthy woman to cheat in a game of bridge in order to win a prize.
 J. For a student to copy from someone else's paper during an examination in a difficult course.
 K. For an unskilled working man to squander his entire week's wages gambling and drinking in a tavern.
 L. For an adolescent to deny breaking a neighbor's large window which he broke accidentally while playing ball.

Four scores are obtained for each subject on each test. Over-all inconsistency, the basic score, is determined by a method outlined by Kendall⁶ which provides a count of circular triads. A circular triad is the result of an inconsistent judgment, such as this: A is preferred over B; B is preferred over C, and C is preferred over A. With 12 stimuli the possible number of circular triads ranges from 0 to 70, the higher score indicating the greater inconsistency. The remaining three scores are functions of decision time. One of these, mean time, is the average length of the period between presentation of stimuli and response. Since a difficult decision normally requires more time than an easy one, a person is expected to respond more rapidly when comparing a stimulus he likes very well with one he does not like than when comparing two stimuli which are about equally attractive to him. In order to determine whether this process was operating, a time-ratio score was computed by dividing the mean response time for the nine judgments involved in comparing the three favorite stimuli with the three least liked by the mean response time required for the 15 decisions involved in comparing the 6 intervening stimuli with each other. The final score, time range, is the difference, in seconds, between the longest and shortest decisions.

Subjects and Administration

The subjects for Designs were 34 state hospital patients who were selected from one large female ward and two male wards which were chiefly composed of recent admissions. All those who participated in this study had been admitted within the

preceding two years, although some had had previous hospitalizations. Twenty-six of the thirty-four were schizophrenics with the sub-categories of chronic and acute undifferentiated, simple, catatonic, and paranoid. The remaining eight were a somewhat diversified group of non-psychotic patients: Six were psychoneurotics; one was afflicted with an acute brain syndrome, and the other was a sociopathic personality. In addition to the psychiatric diagnosis, two had also been alcoholics. Since these patients cannot be subsumed under any medical classification, they shall be denoted as diversified. A comparison of the two groups, schizophrenic and diversified, constitutes the basis of the study.

The patients' cooperation was requested on the grounds that they would be helping in a research on color preference, and only those who were willing to participate without further urging were included in the study. Honest assurance was given them that the results would in no way affect their status in the hospital. Obviously, they did not know that the primary purpose was to measure the consistency of their judgments. Although no standard test for color blindness was administered, all patients stated that they had no color deficiency, and all were able to identify the primary colors. A stop watch was used for measuring time, which was recorded to the nearest second for each response. In addition to Designs, the Wechsler-Bellevue Vocabulary test was administered to each patient at the same session.

The degree of similarity between the groups on four variables which are usually considered influential in psychological testing is indicated by Table 1.

Matching is most satisfactory for education, thus suggesting that at one time the intellectual potentials of the two groups were fairly near equal. Although the difference between the groups in the Vocabulary score does not obtain statistical significance, one hesitates to attribute this to chance, for reduced scores on intelligence tests have often been noted as a result of schizophrenia. With larger groups the same tendency would have reached significance. The diversified patients were significantly older than the schizophrenics, and there were relatively more male subjects in the schizophrenic group. The possible effects of these

TABLE 1.—Descriptive Information Regarding Groups

	Sex		Age, Yr.		Education, Yr.		W-B Vocabulary	
	M	F	Mean	Range	M	Range	M	Range
Schizophrenic	15	11	30	18-47	10.5	4-17	18.3	9.5-26.5
Diversified	4	4	38	19-55	10.2	7-17	21.4	12.0-33.5
Diff.			8		0.3		2.9	
t			2.20				1.17	
P			< 0.05		n. s.		n. s.	

INADEQUACY IN SCHIZOPHRENIC PATIENTS

TABLE 2.—Comparison of Means

	Designs					Social Situations				
	N	Inconsistency	Mean Time, Sec.	Time Ratio	Time Range, Sec.	N	Inconsistency	Mean Time, Sec.	Time Ratio	Time Range, Sec.
Schizophrenic	26	35.0	3.37	0.93	7.8	17	30.8	10.77	0.91	23.8
Diversified	8	16.8	2.84	0.83	6.2	6	11.7	7.61	0.76	18.7
Diff.		18.8	0.55	0.10	1.6		19.1	3.16	0.15	5.1
C		30.5	101.5	72.5	101.5		23.5	44.5	27.0	50.0
P		<0.01	n. s.	n. s.	n. s.		<0.10	n. s.	n. s.	n. s.

factors on the inconsistency score will be considered in the discussion of results.

A week or two after the administration of Designs and the Wechsler-Bellevue Vocabulary, Social Situations was given to as many of the same subjects as were available and to one additional schizophrenic patient. Lack of availability was due to the following causes: discharge, employment by the hospital, ground leave, language deficiency due to a foreign background, refusal to cooperate, low score on the Wechsler-Bellevue Vocabulary, and apparent difficulty in reading. Although the numbers were reduced to 6 for the diversified group and 17 for the schizophrenic group, descriptive information regarding the larger groups was not greatly altered.

Results and Comment

The means of the four scores on the two tests and a comparison of the groups on these values comprise Table 2. Nonhomogeneous variances and skewed distributions ruled out the use of parametric procedures; so all comparisons were made by means of the Mann-Whitney U-test.

Although the difference in consistency between the groups is about the same for the two tests, the smaller number (N) and greater variability for Social Situations prevent it from reaching the high level of significance noted for Designs. It is interesting that the difference between the groups is similar, even though one test requires aesthetic judgments and the other requires judgments regarding human behavior. Although the material in Social Situations is fundamentally more important, it is not im-

mediately relevant with the life situation and may have been viewed quite objectively. Perhaps statements dealing with the social problems of a state hospital would have been more disturbing to all subjects and would have produced different results. In any event, a loss in the ability of schizophrenic patients to make judgments that can be relied upon appears clearly in these data. This observation is far from novel, for victims of schizophrenia at times actually state that they do not know what they think. However, methods for quantifying this loss have been somewhat limited, and one of the purposes of the present research is to suggest a new approach to the problem.

To determine whether the unequal matching of the groups in sex, age, and Wechsler-Bellevue Vocabulary score contributed to this difference, the following computations were made. The means for male and for female subjects were determined separately for each group, and in both instances the male subjects received slightly better scores. Consequently, the greater proportions of male patients in the schizophrenic group would tend, if anything, to improve their scores. Correlations within the groups were calculated to provide an estimate of the influence of the other two variables. These are presented in Table 3.

Since none of the correlations achieve statistical significance and the direction is not consistent for either age or vocabulary,

TABLE 3.—Pearson r Correlations Within the Groups

	Inconsistency Vs. Age			Inconsistency Vs. W.-B. Vocab.		
	r	df	P	r	df	P
Schizophrenic	-0.23	24	n. s.	-0.21	24	n. s.
Diversified	0.58	6	n. s.	0.17	6	n. s.

TABLE 4.—Comparison of Variances

	Designs				Social Situations			
	N	Incon- sistency	Mean Time, Sec.	Time Ratio	N	Incon- sistency	Mean Time, Sec.	Time Ratio
Schizophrenic	26	284.5	4.38	0.031	17	402.6	81.96	0.038
Diversified	8	49.1	1.12	0.021	6	64.7	2.61	0.015
F ratio		5.8	3.9	1.5		6.2	31.40	2.5
P		<0.05	<0.10	n. s.		<0.10	<0.01	n. s.
				n. s.				n. s.

it is probable that the effect of these variables on the inconsistency score was slight.

Although the schizophrenic patients are slower than the diversified patients, and have a higher time-ratio score and a greater range on both tests, in only one instance, time ratio on Social Situations, does this difference approach significance. All those scores, however, are in the expected direction.

A difference between means might be due to a displacement in one direction, or it might be due to a greater range, with the distributions equal at one extreme and unequal at the other. Furthermore, similarity between means does not necessarily imply similarity in ranges. To investigate further the differences between the groups, comparisons were made of the variances of the four scores, and these are given in Table 4.

Again, we see rather similar results for the inconsistency measure on the two tests. The reason for the increased variance for the schizophrenic patients is that nine of their members on Designs and eight on Social Situations had scores in the range of the diversified population, while the others had more deviant scores. This is similar to, although slightly higher than, the percent of overlap reported by David and Rabino-witz¹ in a comparison of schizophrenic patients and student nurses on judgments regarding the Szondi pictures by a test-retest procedure. With one exception, there was a definite tendency for the schizophrenic patients who did well on one test to do well on the other test. Three of the nine schizophrenics with the good scores on Designs were not included in the population for Social Situations. One of the remaining six did very poorly on Social Situations, but

the other five received the five best scores of the schizophrenic group. Of the three remaining schizophrenic patients who reached the diversified range on Social Situations, one was not included in the population for Designs, and the other two were at about the mean for their group. To investigate whether or not scores on these tests are in any way related to the various types of schizophrenia, or whether they have any implications for prognosis, would provide an interesting research. Furthermore, studies could be designed to determine whether those who received scores in the diversified range have a greater capacity for taking responsibility than the others.

With mean time, time ratio, and time range the increased variability of the schizophrenic patients is generally due to a few excessively high scores; however, on Designs the nine shortest mean times were also achieved by schizophrenic patients. The scores of two subjects for mean time in Social Situations who were extremely slow were responsible for the great variability of the schizophrenic group. Since the time scores are not entirely independent, only a very general interpretation can be given. It seems that among the schizophrenic subjects there are different ways of responding when the patient is faced with a difficult decision. Some wish to avoid the issue and consequently respond very rapidly without giving the problem any consideration, while others, although not able to choose as quickly, or perhaps as consistently, as better-integrated people, devote much time in an attempt at a careful decision. This difference in behavior may provide some insight in a clinical evaluation.

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TABLE 5.—Results of Paired Comparison Analyses

Designs				Social Situations			
Schizophrenic		Diversified		Schizophrenic		Diversified	
Stimuli Rank	Standard Score	Stimuli Rank	Standard Score	Stimuli Rank	Standard Score	Stimuli Rank	
D	1.104	D	1.489	E	0.997	E	
L	0.794	B	1.304	K	0.690	K	
F	0.737	F	1.301	G	0.648	G	
J	0.725	C	1.045	L	0.453	I	
A	0.623	A	0.830	J	0.446	J	
C	0.497	L	0.783	H	0.357	D	
H	0.446	J	0.761	C	0.320	C	
B	0.418	K	0.666	D	0.264	H	} Tied
E	0.408	G	0.444	A	0.150	A	
G	0.338	H	0.358	F	0.106	B	
K	0.146	I	0.194	B	0.103	L	
I	0.000	E	0.000	I	0.000	F	

Both Designs and Social Situations were administered to a group of nonhospitalized controls, who were better educated and apparently more intelligent than either of the patient groups. Their scores were very similar to those of the diversified patients, thus again suggesting that within the normal range intelligence is not an influential factor in determining the consistency of judgment as required for these tests.

Although the content of the items was not of primary interest in this study, another type of comparison between the groups was made available by scaling the items by a traditional method of Paired Comparisons. The treatment employed was Case 5 with unweighted scores, as described and illustrated by Guilford.³ This analysis was not completed for the diversified group on Social Situations, for their number was very small and in many instances all subjects chose one stimulus over another, thus giving rise to too many indeterminant values for reliable results. However, the order of choice for these data is presented in Table 5, with the findings of the three paired comparison analyses.

In each test there is both a noticeable similarity between the groups and one rather marked shift. In Designs the schizophrenic group chose L second and B eighth, while the other group chose B second and L sixth. The predominating color in D, which was chosen first by both groups, is light green. A green with a shade similar to grass is the chief color in L, while B is mostly red. A preference for green, or an aversion to red,

or both, on the part of the schizophrenic patients might be responsible for this result. The order for the first three items is identical for the two groups in Social Situations. Statement E ("for an employee to sneak inexpensive items away from his office and use them in his home"), which was considered worst, may have been viewed as stealing, and, as such, a crime punishable by law. In general the other statements describe types of social behavior which are censored only by social attitudes. It would be audacious even to attempt an explanation for the perfect agreement between the groups in choosing K and G as the second and third items. The reason for the almost complete reversal of I and L, both of which pertain to honesty, is also not clear. Perhaps the destructiveness involved in breaking a large window is more frightening to schizophrenic patients, who often fear self-destruction, than it is to the diversified subjects. For this reason they may have tended to judge it worse, although "the lying," and not "the breaking," was intended the basis for judgment.

In Designs the range is somewhat greater for the nonpsychotic group. The higher within subject consistency is probably the primary factor responsible for this.

Summary and Conclusions

The aim of the study was to develop tests which would provide scores that quantify the ability involved in making consistent judgments, and to compare schizophrenic and diversified nonpsychotic state hospital

patients on the basis of these tests. An analysis of the test scores led to the following conclusions regarding the two groups of subjects:

1. There is a very significant difference between schizophrenic and diversified non-psychotic state hospital patients who are roughly matched for age, education, and Wechsler-Bellevue Vocabulary in their ability to render difficult discriminations.

2. Slightly over one-third of the schizophrenic patients received scores in the range of those of the other subjects. A comparison of the present capacities and future adjustment of those who scored in this range and those who performed less adequately would provide an interesting investigation.

3. An analysis of the time scores which show that some schizophrenic patients ponder an excessively long time on a difficult decision, while others give almost spontaneous, uncritical responses, might contribute useful information to a clinical evaluation.

4. There seems to be a reasonable amount of similarity in order of choice of stimuli between the two groups in the type of items used in both tests.

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Psychotherapy with Ambulatory Schizophrenic Patients in Mixed Analytic Groups

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Introduction

There is a large body of literature dealing with group psychotherapy as applied to psychotic, in their large majority schizophrenic, patients and practiced mainly in state and Veterans' Administration Hospitals and their outpatient departments (Breckir, Geller, Low, Hulse, and others). This type of group psychotherapy practice is geared to the psychotic symptomatology of the patients and uses mainly repressive or generally supportive features for the improvement of the patients' acutely psychotic condition and for the better handling of hospital routines.

The purpose of this presentation is basically different from the above-described procedures, as we are geared toward a dynamic, psychoanalytically oriented treatment process directed at the basic psychodynamics of emotionally disturbed human subjects.

This paper reports on the application of psychoanalytically oriented group psychotherapy to ambulatory adult schizophrenic patients. The groups are organized in the private psychiatric office or in hospital outpatient clinics. The therapeutic group is composed of six to nine carefully selected patients of either one or both sexes; the majority of the patients are suffering from psychoneurosis or character neurosis. Only a very small number of patients (one or two) with schizophrenia are admitted to each group. Groups meet once or twice weekly for 90 to 100 minutes. The majority of the patients receive group psychotherapy exclusively, but provisions for

concomitant individual therapeutic sessions are made. This type of psychotherapy can, and often has to, be applied continuously over one or several years, even if the composition of the group changes during the treatment period of a specific patient.

The Schizophrenic Patients in Mixed Analytic Groups

If we consider schizophrenic patients for analytic group psychotherapy together with psychoneurotics, we have to state our concepts in the use of the word "schizophrenia" and its various derivatives, like "schizoid," "borderline," and so on. We do not intend to include here the different uses of the term "childhood schizophrenia," as children cannot be treated by the type of group psychotherapy used for adults under discussion.

Schizophrenia is an illness with very definite characteristics, which in most cases can be diagnosed with a good amount of certainty clinically, as well as through projective testing, in psychotic as well as in nonpsychotic patients. That means that a schizophrenic patient, as defined by Bleuler, does not have to be psychotic, does not have to have had a previous psychotic episode, and might never in his life lapse into a psychotic state. This concept is today fairly generally accepted, and we therefore differentiate between psychotic and nonpsychotic schizophrenics, with the understanding that there is not always a sharp dividing line; but there are large numbers of patients with schizophrenia who are definitely psychotic, and there is also a definite number of schizophrenics who are definitely not psychotic but who are seriously ill. There is an in-between group of patients who have been

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psychotic and are in remission or whose psychosis has been suppressed through ataractics, electroshock, or insulin coma. Some are in continuous remission; others are definitely cured of their schizophrenic psychosis. There are patients concerning whom even a very experienced clinician or a very experienced projective technician might at times not be quite sure whether they are or are not in a prepsychotic state or whether they are actually psychotic.

To these doubtful groups belong patients with the so-called "pseudoneurotic schizophrenias" and the so-called "borderline" states. Their strong psychoneurotic-like defense mechanisms would classify them among the nonpsychotic schizophrenics or in the in-between group who might or might not at certain times develop psychotic manifestations. We prefer a primary differentiation of psychotic and nonpsychotic schizophrenic states and shall then use subclassifications according to the presenting symptomatology in nonpsychotics—pseudoneurotic schizophrenia, simple schizophrenia, postpsychotic schizophrenic state, schizophrenic character disorder, etc. (The well-established classification of the psychotic schizophrenic states, such as hebephrenic, catatonic, mixed, and paranoid, will, of course, be used.) The designation "borderline" seems a very confusing and inadequate use of terminology and will be avoided. We should also like to reserve the term "schizoid" for those "normal" character traits and behavior attitudes that are somewhat reminiscent of schizophrenic pathology but are regularly observed in healthy persons without need for therapy.

Many group psychotherapists feel that the nonpsychotic schizophrenics (with the exception of the defective postpsychotic patients) can be accepted for analytic group psychotherapy. Whether they can be cured by the application of this method or by a combination of individual and group psychotherapy is an open question. They certainly respond well to either group psychotherapy alone or a combination of

group psychotherapy and individual psychotherapy. They usually accept the group better and stay willingly over longer periods of time in groups than with any other psychotherapeutic approach.

It is difficult to describe their over-all behavior in the group because there is a large variety of manifestations of their schizophrenic disorder. They often display hostile, aloof, distant behavior; others appear to be frightened people, submissive and shy, with many whiny complaints about everything going wrong. Very often schizophrenic patients are, in their aloofness, very righteous, take arbitrary attitudes, and pretend to know the answers to all questions. While wanting to appear as very superior persons, they actually display poor judgment about their achievements in life and in their attitudes toward themselves and toward others.

They have brittle personalities and avoid anxiety by dropping out of treatment if the therapist forces them prematurely to face anxiety-provoking material. They have to be protected against early exposure in the group therapeutic process; this protection can be achieved by an experienced and sensitive therapist through the subtle use of other group members in helping to protect the brittle patient; this is a superior technique as compared with a group constellation where the therapist has to carry out such tasks by himself. A well-functioning group acts frequently as a body for the defense of a specific, anxious member with schizophrenic traits. All patients in a group use each other as defense against too great an exposure of their own conflicts in anxiety-loaded areas; for them, the group is a protective agent, a safety device in their brittle operations in living.

Many ambulatory schizophrenics, especially the hostile, aloof, righteous type, are, on the other hand, often provocative and sometimes attract a great deal of hostility from the group; they become a kind of scapegoat in groups where many members are afraid to attack directly the real target,

namely, the therapist. If the therapist understands that, although they attack one another, they actually mean the therapist, he can then make therapeutic use of this situation. He can protect the frightened, passive-aggressive schizophrenic in the group by offering himself as a target. Later he may interpret the dynamics of the men's "revolt against the father" and the women's "fight for the father."

These situations are some rather complicating factors produced by the presence of schizophrenic patients in the group, but there are also very definite positive aspects. As mentioned before, the patient can be kept in a prolonged therapeutic process in which his very weak and brittle ego will find continuous support from his peers, represented by other group members and by the group as a body. This support enables him to handle his own anxieties better. Thus, in the long run, he will loosen up his rigid ego defenses, which otherwise make the treatment of this type of patient so extremely difficult. The next step in his improvement will be fewer ego-restricting, self-castrating and self-punitive mechanisms, better social contacts, less aloofness, and greater ability for warmth in interpersonal relations.

The schizophrenic very often makes a great and valuable contribution to the group process by his ability to let his unconscious speak up in the group and by his tendency to make very lucid statements about ego-threatening feelings and ego defenses. These statements often apply to all human beings. The group process becomes very stimulated, and the neurotics in the group are provided with extremely valuable material for the development of insight. While this process helps the psychoneurotic patients in the group to gain permanent insight, the schizophrenic's own lucid insightful attitude very often gets lost. After a short while he hardly remembers; and, if he remembers, his previous statements become meaningless to him. He has the mechanism for insightful, lucid statements, but the process of integration takes much longer or is not available

to him to the extent to which the psychoneurotic patient can use it.

The foregoing might be illustrated by a brief description of a group experience. Our patient, an unmarried woman of 30, had previously been treated for two years, without success, by modified psychoanalysis, three or four sessions per week. At the time she was referred for group psychotherapy, she had not been able to work for several years, since she had broken down with rather vague physical and emotional symptoms, at first diagnosed as an industrial disease, caused by a chemical agent she had been using in her work.

During individual analytic treatment her illness was correctly diagnosed as a chronic schizophrenic process. There was severe early ego damage: She had never known her father; she had migrated with her mother through many countries, with frequent environmental changes in their unsteady, marginal existence; the mother, a strong-willed but emotionally unstable person, gave her daughter early a great deal of information about her own disturbed and bizarre premarital and marital experiences and her poor emotional and sexual adjustment in later life.

The patient herself had had a number of emotionally ambivalent, casual sexual contacts before she came into group treatment. Abandonments, cruel handling, and abortions had left her extremely frightened about relationships with men. We shall not describe here in detail the many schizophrenic features of this nonpsychotic patient but shall present only one specific situation that occurred in a group of eight women which the patient under discussion had then attended for about 18 months, with definite progress: She was then working steadily, had expanded her social relations, and had been a fairly active participant in the group. During a very active and intense discussion about unsatisfactory sexual relations, she said that she had never had satisfactory orgasmic experiences but that she thought that she could have orgasm; she had frequently been very aware in her sexual relations of the beginning of orgasmic feelings, but she felt that she was going to "get lost," in orgasmic feelings, that she would lose herself, her identity, and that she was so frightened about this that she had to make a conscious effort not to continue because she could not imagine how, if she "ever lost herself" in orgasm, she would ever "come back." She feared that she would "go to pieces," that each piece would remain separate, and that she would never get herself together again.

It would be difficult to find a psychoneurotic unable to achieve orgasm who would be able to verbalize so lucidly the threat to the ego that orgasm represents to many patients. The orgasmic experience is actually

a momentary total loss of ego awareness and ego conceptualization. Several other group members agreed with her and showed excitedly their amazement that she could describe so well why they did not have orgasm, what happens, and what threatens them in their own ego structures. She had been able to verbalize a deep emotional experience, but, unfortunately, this is where her case rested; she could not go any further. She had helped enormously the neurotic patients who, by identifying with her, could now understand what it was that limited their own sex life. Some of them were able to understand this emotionally and to work it through. They were able after several weeks or months to say: "Now I could have orgasm, knowing that I would not go to pieces, and I would come out of it again whole and as a complete person." The schizophrenic patient could not achieve this with the psychoneurotic patients. She could have a flash of insight, but the integration of this insight was much more difficult for her. She continued to improve steadily but dropped out of the group one year later, when she got into a panic state over a love affair while she was deprived of support by the group, when it was on its six weeks' summer vacation. Patients of this type really depend on a continuous therapeutic experience over a period of many years; they should never have a vacation from therapy. Unfortunately, this is technically nearly impossible.

This case illustrates how this type of schizophrenic patient can make a great contribution to the group but how slowly the patient himself gains ego strength through the process. These patients often exhibit very great resistance toward awareness and verbalization of any emotional attachment to group members or to the therapist. They deny over long periods of time insight into transference phenomena. They later give up this resistance under the continuous and insistent impact of the other group members, who, by manifesting their own emotionality and by interpreting each other's transference

symptoms, demonstrate to the schizophrenic in a kind of inductive process that the schizophrenic's own behavior, his dreams, and his free associations represent actual transference phenomena which the patient does not want to, or is not able to, recognize.

With the one or two nonpsychotic schizophrenics whom a group can carry might be included also one postpsychotic schizophrenic if he does not show deterioration. The therapist has to be careful not to include too many because of their frequent need to be protected against the anxiety, hostility, and aggression of the other patients. Most careful and responsible therapists usually cannot watch closely, protect, and treat more than one or two such patients in a group of seven to nine.

Schizophrenics with rare psychotic episodes, maybe a single episode some years ago, do not have to be excluded just because of this history, but the patient's present state and total personality make-up have to be carefully evaluated. If a patient who has had previous psychotic episodes and had been accepted in a mixed group during remission becomes psychotic again, he frequently cannot be carried in a group and has to be taken out of the group. This is something to which we all are exposed in our therapeutic planning. Not always does the patient act or respond as we expect him to respond. We should not be rigid, should admit our error, and should change our treatment plans in such a case. While we have to learn from our mistakes, we shall never be able to avoid all mistakes.

We should also recognize that psychotic episodes do not occur exclusively in schizophrenics, and we should not make the diagnosis of schizophrenia solely on the basis of a presenting psychotic state. Psychosis as a clinical picture is not reserved to schizophrenics. Many war, and especially combat, experiences have proved that everybody has a threshold for psychotic breakdown and that if this threshold is overstepped, everybody can become subject to a psychotic episode. One does not have to be schizophrenic

for this. Of course, the schizophrenic psychosis exhibits a specific coloring and does not show the tendency to early spontaneous recovery which the majority of other psychotic episodes have.

It is, in general, not advisable to take into analytic group therapy schizophrenics who are inclined to verbalize freely hallucinatory or delusional material. Such an experience may be disturbing to the other group members, and it may be difficult to handle such material in a group. The same is true for paranoid patients, but the very presence of some paranoid or delusional material in the verbal output of a patient during diagnostic interviews should not be considered sufficient for definite exclusion of such a patient from group psychotherapy. Moderate paranoid attitudes are not completely unknown as temporary symptoms in many types of severe psychoneurosis. These patients produce temporarily material that is delusional, and even hallucinatory, while most of the time they maintain adequate contact with reality. It is the latter clinical aspect that is most important if one selects such patients for group psychotherapy.

That it is possible for psychotic schizophrenics, including paranoid types, to maintain situationally adequate contact with reality and to suppress over long periods of time successfully hallucinatory and delusional material is well known. The therapeutic group seems to exert a very strong stimulus toward such efforts of a very sick patient to maintain and to strengthen his hold on reality. We have had the occasion to observe this in an analytically oriented group.

The patient, Miss X., is a paranoid, psychotic schizophrenic with a long history of active illness. She has very high intelligence and high academic achievements, doing research in a scientific field. She had been actively hallucinating, with ideas of reference and feelings of persecution, for at least five years while she was under individual therapy with three different psychiatrists. There had not been any doubt about the correctness of the diagnosis; she had left each of her therapists under dramatic circumstances after prolonged treatment periods and had followed up her leaving by

making innumerable anonymous telephone calls to them, under annoying circumstances. She was tentatively accepted in an emergency for combined individual and group therapy. As she behaved in an extremely anxious and hostile manner in individual sessions, but much less so in the group, and as she insisted that she liked and wanted group psychotherapy, she was treated only by group therapy for nearly two years.

The group was an all-female one of seven, in which she showed considerable symptomatic improvement. She was more reality-oriented in her everyday life, had better social relations, was less quarrelsome at home and in her work, and was able to carry out a qualified teaching job in addition to her research. She started out in the group with the same high degree of anxiety and hostility that she had shown previously in the face-to-face situation of individual therapy. But while she had always had bizarre delusional, hallucinatory, and strongly paranoid thinking and never had hesitated to verbalize it in her many years of individual sessions, she produced only moderately deviate thinking in the group—very rarely and usually only in the form of dreams or pseudodreams, or comments on the dreams of others. We had the opportunity to discuss her progress with her former therapists. There was general agreement that she had never done as well before as she had in this group, where she was treated together with psychoneurotic patients.

This patient has said repeatedly in the group and to the therapist over the telephone that she felt that she "belonged," that she was less tense in the group than she was in her daily work, and that she thought that this treatment was the best she ever had. She has never been openly disturbing in the group.

There were occasionally some disturbed reactions noticeable in her relations to other group patients. Another group member, Mrs. Y., had a great deal of latent homosexual fears. These two patients got at times into hostile interchanges with each other, which grew out of a reality relationship, for it came out during the treatment that they had worked at the same time in the same company several years before. This, of course, was upsetting to the psychotic-paranoid Patient X. The other patient, Mrs. Y., had once a dream that she was raped by a man on a dark stairway, and that the physical description of this man fitted Miss X. very well, including some characteristic, facial disfigurements.

A week later, i. e., in the following session, Mrs. Y., in an association to the dream, became aware and said that the rapist reminded her of Miss X. Miss X. was very upset—why should Y. dream of her as a male? This opened up discussions about latent homosexuality and the representation of repressed sexual desires in dreams. Both patients,

together with other group members who now remembered their own homosexual dreams and thoughts, accepted interpretations and explanations. Not at any time did this material become traumatic for any of the group members, nor did it disrupt the therapeutic process. This case material cannot and is not intended to prove that paranoid psychotics should be treated routinely in psychoanalytic groups of psychoneurotic patients. But the case shows that such procedure can give good results. Miss X. left group therapy after about two years, when her own group was discontinued; but she kept friendly relationships with certain group members, whom she called up over the telephone. She is reported to be doing well, two years after discontinuation of treatment.

Comment

The two patients presented on the previous pages represent the severest cases in our large material, observed over a period of up to 10 years. Many less acutely ill patients with the type described by Bleuler as "schizophrenia simplex" or as "latent schizophrenia" have been and are presently treated in our groups. Not only do they show the character traits of "irritable, odd, moody, withdrawn, or exaggeratedly punctual people" (Bleuler) with hypochondriacal, alcoholic, querulous and other symptomatology but they often came into therapy during acute exacerbations of their chronic schizophrenic character illness, such as acute panic in response to homosexual threat or homicidal and suicidal confusion states following childbirth.

Our results have been most gratifying in those patients who develop enough insight and transference relations to remain in group psychotherapy for extended periods of time (four to five years). The therapeutic setting has to make allowance for concomitant individual sessions during part of the treatment period (either in regular intervals or whenever the acute therapeutic situation demands additional sessions). I have, in a previous paper, pointed to the superiority of this type of "combined" therapy in the development of transference reactions in patients with serious types of deep-seated character psychopathology, especially chronic schizophrenic states (Hulse).

Under the impact of multiple identifications and transference-like reactions to other group members, these patients are able to lessen the strong and crippling hold which their rigid defenses have on their ego. In the group, an extremely complicated dynamic interplay seems to permit these patients with severe psychopathology the acceptance of interpretative material to a much higher degree than we can observe it in individual analytic sessions. The manifestations of homosexual drives and the following panic reaction find a surprising amount of identification and tolerant acceptance from the psychoneurotic group members as long as the therapist himself does not become emotionally affected by the outpouring of socially prohibited material in group sessions.

The acceptance of verbalization of violent id impulses is often promoted by the greater reality closeness of the group atmosphere, which enhances the tolerance level toward threatening prepsychotic material in individual psychoneurotic patients. Intact intellectual functioning is of great importance but is not absolutely required during all phases of the treatment course.

We have had occasion to observe a very intelligent college student with severe ego pathology of the schizophrenic type who entered the group in a psychotic state (group sessions were at that time combined with individual therapy) following childbirth after a shotgun marriage with a delinquent hobo who had impregnated her. Individual sessions could soon be reduced to a minimum while the patient worked through her many deep-seated childhood conflicts in the group—very often through violent and reality-removed attacks of temper. After five years of intensive group therapy, she has not only recovered to adequate intellectual and social function but has also gained great insight into her personal conflicts. This she is able to communalize to a high degree that makes her a very effective voluntary co-therapist in the group.

The therapeutic group as a dynamic element in treatment is an instrument which

the group therapist has to forge by his skill and judgment. It never becomes fully independent of him, but it also provides him with additional ego strength. The well-composed group is—in a certain way—shock-proof! It is able to absorb a much greater amount of psychopathological impact and provides more resilience than is at the disposal of an individual therapist. The amount of resilience seems to be of great importance for the ego structure of those who are able and willing to undertake the task of treating schizophrenic patients by psychotherapy. There are elements in the integrated therapeutic group which—through continuous changes in the intragroup constellation—protect the group and the group therapist from the accumulation of negative countertransference, and therefore protect the patient against his own destructive tendencies aimed at the therapeutic constellation. The elements of balance and buoyancy manifested in the group process can act equally well in dealing with the group therapist's positive countertransference reactions, which are early exposed and made conscious by the watchfulness and competitiveness that are part of the "belonging" of the individual in the group.

The results obtained during the past 10 years in psychoanalytically oriented psychotherapy with schizophrenic patients in mixed groups prove that a valuable new weapon has been added to the small, but growing, armamentarium of dynamic therapeutic methods for the rehabilitation of ambulatory schizophrenic patients.

Summary

A new group psychotherapeutic method for the treatment of schizophrenic patients is described.

The majority of schizophrenic patients eligible for this type of group psychotherapy belong to the not-actively psychotic categories; i. e., they are pre- or postpsychotic patients whose disorders were diagnosed as so-called borderline states (pseudoneurotic schizophrenia, simple schizophrenia, latent

schizophrenia, or schizophrenic character disorders). In a few instances psychotic patients with delusional and hallucinatory states were admitted and responded well.

Case material shows that the majority of the patients selected for this kind of therapeutic approach responded well and showed decrease of depressive and fearful feelings, greater closeness to reality, increased social activity and responsibility, and improved interpersonal relations. A certain percentage of failure, even among carefully selected patients, is reported. An attempt is made to clarify the psychodynamics of this therapeutic approach and to show actual contributions which the schizophrenic patients can make to the treatment of the neurotic group members.

350 Central Park West (25).

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A Quantitative Method of Estimating Variations in Intensity of a Psychologic Conflict or State

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The problem of estimating the relative intensity of a psychologic conflict is an important and challenging one for investigators of human personality. One aspect of this problem, which has been particularly elusive, has been that of comparing the intensity or degree of a specific psychologic conflict in one patient at different times and over a large number of periods of observation. Investigators attempting to evaluate the effect of therapeutic agents or procedures, e. g., drugs, electroconvulsive treatment, and psychotherapy, have felt the need for a precise and reliable technique of measurement of changes in psychodynamic balance within a subject. The need has also been felt by investigators doing psychosomatic studies.

The development of personality tests and inventories has been one approach to this problem, but most of these methods, while capable at their best of distinguishing reaction types among a group of individuals, are not sensitive enough or are not so constructed as to make fine discriminations of the full range of variations within an individual. Furthermore, another approach, the psychiatric rating form, though it attempts to measure variations within an

individual, as well as differences among individuals, has not usually been tailored to give information about psychodynamic relationships, and often the reliability of the procedure has not been established.

This report describes an experimental method of estimating the intensity of a psychologic state by means of frequency counts of relevant categories of references occurring in samples of speech plus the application of this method to a problem in psychosomatic correlation. The present study is part of a program of research on the analysis of verbal behavior in which a group of investigators is collaborating.¹⁻⁵

In a preliminary study⁶ an association was noted between the intensity of a specific psychodynamic state of a 32-year-old woman and the relative percentage of *Streptococcus* colonies cultured from her oropharynx. It appeared in that study that there was an association between the bacteriologic variable and the ways in which the patient was attempting to handle her inordinate dependent yearnings. On the one hand, she wanted to get love and attention but tended to inhibit the direct expression of these dependent wishes because she felt undesirable, unworthy, and likely to be spurned. On the other hand, she became resentful at the frustration of her cravings but avoided expressing directly her reactive hostility for fear of further alienating potential sources of affection and attention. Our preliminary study suggested that when the patient was attempting to resolve her conflicts by the compromise of accepting or seeking punishment and the enhancement of suffering to gain support, attention, human contact, the *Streptococcus* colony counts in

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her throat cultures tended to be very high. When she was attempting to resolve her conflicts without using such masochistic devices and when she was finding herself a more worth-while person, these bacterial colony counts were relatively low. These findings led to the formulation of a hypothesis concerning psychophysiological relationship within this one patient that we then sought to validate in the observations reported in this paper. Our hypothesis was that the more subjectively unsatisfactory and unsuccessful this patient's compromise problem-solving techniques were, particularly masochistic ones, toward resolving her insatiable urges for attention, support, and respect, the higher would be the percentages of *Streptococcus* bacteria in her throat.

Method

A technique of obtaining throat cultures in a standardized and reliable way had already been established.⁷ Each weekday for 20 days the patient, who was residing on the Psychosomatic Unit of the Cincinnati General Hospital, went to the Microbiology Laboratory, where a throat culture was obtained.

Immediately after the obtaining of each throat culture, the patient returned to the Psychosomatic Unit, where a sampling was taken of the status of her psychologic conflicts. The method of sampling consisted of having the patient speak, without verbal comment or interruption by the interviewer, for a period of five minutes about any dramatic or personal life experience she ever had or was having.^{1,8} The verbal samples were collected in a quiet room with only a woman technical assistant present, and the patient's speech was recorded on an electronic tape recorder. The verbal material was typewritten and then analyzed for its content. Thus, 20 such five-minute verbal samples, matched in time of sampling with 20 throat cultures, were thus obtained, one of each on nearly a daily schedule for 20 days.

Our patient's adjustment difficulties were seen, as previously mentioned, as stemming from urgent desires to be loved, and in the service of this need she had a cluster of interrelated problem-solving efforts, which in themselves were variously blocked from succeeding. The more unsatisfied she felt, the more in desperation she used methods of reaching her goals that brought suffering and pain as the price of attention and human contact. It was conjectured that if a tally could be kept on all

facets of this whole interrelated system of aims and conflicts, and an actual count made of her more successful and less successful efforts, as well as her more pleasurable reactions and less pleasurable reactions moment by moment, an estimate might be obtained that would indicate what was the resultant of these various inner forces.

In analyzing and scoring the five-minute samples, we had to make a number of assumptions, the justifiability of which, we felt, would in part be tested by how accurate our predictions turned out to be. First of all, we assumed that a subjective experience (drive, counterdrive, affect, and so forth), as it is refined during the cognitive processes preparatory to the act of speech, is reflected in the content of units of speech. Our impression was that the smallest communication unit that conveys essential information in our language about process, agent, and object is the clause, the combination of a subject and predicate, although in some utterances, as with interjections, either one or both of these elements are omitted but understood through conventional usage by speaker and audience. Accordingly, each of the verbal samples was broken down into its component clauses.

Our next assumption was that the frequency of references made by the patient per unit of verbal communication (clause) to ideas, emotions, sensations, and activities commonly indicating distress, suffering, disapproval, diffuse resentment, frustration—for the most part regardless of agent, object, or time—would indicate the amount of currently unsuccessful and unsatisfying compromise solutions, particularly masochistic ones. Each time such references would occur in a clause, they were scored -1 . On the contrary, the frequency of references indicating self-reliance, success, achievement, increased self-esteem or well-being, open repudiation of her physician, and painless reception of supplies of affection and attention was assumed to reflect the amount of successful and satisfying problem-solving thought processes of the moment. Each time such references occurred they were scored $+1$. We speculated that the algebraic sum of all these plus and minus scores, corrected for the number of words spoken in each sample, might give us a rough measure of the current over-all emotional state of our patient.

We shall now describe our procedure in more detail. There were 10 specific content categories that we used in this system of verbal analysis (Schedule). The first six were considered to be categories of references which, we thought, would most likely be verbalized when the patient was using ineffective and masochistic solutions to her dependency conflicts and when the total *Streptococcus* percentage was elevated. Category 6, however, was one which we were uncertain had

SCHEDULE

Thematic Coding System for Scoring Emotional Conflicts Associated with Oropharyngeal Flora

- | | | | | |
|------------|--|----------|------------|-----------------|
| (score -1) | 1. Experiencing suffering, injury, punishment, physical or emotional complaints, discomfort: | (a) self | (b) others | (c) unspecified |
| (score -1) | 2. Feelings of depression, guilt, shame, experienced by: | (a) self | (b) others | (c) unspecified |
| (score -1) | 3. Adverse criticism, neglect, hostility, rejection, loss, abandonment by others to: | (a) self | (b) others | (c) unspecified |
| (score -1) | 4. Same as Category 3, but by self to (and excluding Category 9): | (a) self | (b) others | (c) unspecified |
| (score -1) | 5. Sexual activity or wishes, seductiveness (to win care, support) by: | (a) self | (b) others | (c) unspecified |
| (score -1) | * 6. Blocking, difficulty in performing, producing, giving, expressed by: | (a) self | (b) others | (c) unspecified |
| (score +1) | 7. Independent strivings, enjoyment of success, achievement by: | (a) self | (b) others | (c) unspecified |
| (score +1) | 8. Feelings of self-esteem, well-being, experienced by: | (a) self | (b) others | (c) unspecified |
| (score +1) | 9. Open expression of hostility to interviewer or therapist by: | (a) self | (b) others | (c) unspecified |
| (score +1) | 10. Receiving love, attention, affection, gifts, rewards, experienced by: | (a) self | (b) others | (c) unspecified |

* This category was included with the reservations noted in the text.

relevance to masochistic problem-solving techniques, but it was included, with the reservation that either with or without this category of thematic references we could predict when the patient was most in conflict and distress and, therefore, when Streptococcus counts of her oropharyngeal flora were higher. The last four categories of references were those which we felt would most likely be verbalized when the patient was considering or actually trying more adequate and satisfying solutions to her needs and the conflicts they involved and, therefore, when the total Streptococcus percentage was reduced.

Each communication unit—clause—was scored either +1 or -1 if it contained content relevant to any one category, whether the object involved was (a) herself, (b) others, or (c) unspecified persons or objects. Content was scored, also, whether it was expressed in the form of past, present, or future tenses, as conditional probabilities, or in the form of wishes. The rationale for this type of procedure was again an assumption, which has gained some support in another, similar type of study we have carried out,² the assumption being that these different aspects of content are equivalent insofar as they express a subject's current subjective state. A clause was scored more than once if two different categories were present therein. The following excerpt is the first minute of a five-minute verbal sample given by the patient, scored according to our method.

"When I was seven years old uh/ † I can remember at Christmas uh/ because that was the year/ I discovered/ there was no ^{2a(-)} Santa Claus/. And uh uh this is/ it seems sort of odd in a way/ because uh I've told this very same thing to Dr. E—/. And I think uh during these five-minute sessions uh/ I know/ I, I received ^{10a(+)} seven dolls for Christmas/. And uh we had ^{10a(+)} a beautiful ^{10a(+)} tree/. And uh even though it was such a pleasant ^{8a(+)} Christmas/ I, I did find out/ there was no ^{2a(-)} Santa Claus/. And I can ^{2a(-)} remember crying about it/. And uh, well, it just seems sort of funny/ that I should uh think of that the ^{2a(-)} first thing/ and uh at the same time before; that's ^{2a(-)} what I thought of uh/. This is uh uh/ . . . I can't think of anything to say/."

The plus and minus scores in each verbal sample were added algebraically to give a raw score for the verbal sample. Since there were variations in the total number of words the patient spoke during each five-minute period, the raw score for each sample (multiplied by 100) was divided by the total words spoken for this sample to give a final, corrected score for each sample. This score represented the sum of two main types of references (plus and minus ones) occurring per 100 words in each verbal sample. These data are

† Diagonal mark indicates one unit of communication (one clause).

‡ Numbers and letters refer to categories and subcategories listed in the Schedule.

ESTIMATION OF PSYCHOLOGIC CONFLICTS

TABLE 1.—Scores and Rankings of Intensity of Psychologic Conflict Revealed in Each of Twenty Verbal Samples Compared with Rankings of Relative Percentages of Total Streptococci Cultured from a Patient's Throat

Sample No.	Date Obtained	Total Words Spoken	Scores Including Category 6					Scores Excluding Category 6					Streptococcal Colonies	
			Plus	Minus	Combined	Corrected	Rank	Plus	Minus	Combined	Corrected	Rank	Per Cent	Rank
1	7/11	309	3	12	-9	-2.9	10	3	5	-2	-0.6	4	52	4.5
2	7/12	269	0	16	-16	-6.0	19	0	11	-11	-4.1	19.5	52	4.5
3	7/13	553	6	21	-15	-2.7	8	6	11	-5	-0.9	8	55	6.0
4	7/16	610	15	28	-13	-2.1	5	15	18	-3	-0.5	3	72	9
5	7/17	646	14	34	-20	-3.1	11.5	14	27	-13	-2.0	15.5	66	7
6	7/18	413	8	19	-11	-2.7	8	8	16	-8	-1.9	13.5	74	11
7	7/19	303	8	8	0	0.0	1	8	4	+4	+1.3	1	43	1
8	7/20	636	11	24	-13	-2.0	4	11	17	-6	-0.9	8	46	2
9	7/23	365	4	22	-18	-4.9	18	4	10	-6	-1.6	11	50	3
10	7/24	443	11	21	-10	-2.3	6	11	14	-3	-0.7	5.5	73	10
11	7/25	704	5	31	-26	-3.7	14	5	18	-13	-1.8	12	71	8
12	7/26	141	0	13	-13	-9.2	20	0	10	-10	-0.7	5.5	78	12
13	7/27	460	3	24	-21	-4.6	17	3	22	-19	-4.1	19.5	83	18
14	7/30	638	15	35	-20	-3.1	11.5	15	21	-6	-0.9	8	80	13.5
15	7/31	653	15	25	-10	-1.5	3	15	22	-7	-1.1	10	81	15
16	8/1	900	22	27	-5	-0.5	2	22	18	+4	+0.4	2	82	16
17	8/2	519	10	24	-14	-2.7	8	10	20	-10	-1.9	13.5	80	13.5
18	8/3	640	11	38	-27	-4.2	16	11	32	-21	-3.3	18	86	20
19	8/6	784	6	33	-27	-3.4	13	6	22	-16	-2.0	15.5	83	18
20	8/7	132	2	7	-5	-3.8	15	2	6	-4	-3.0	17	83	18

$\Sigma d = 1060.$
 $r_s = 0.20.$
 $P < 0.05.$

$\Sigma d = 787.$
 $r_s = 0.41.$
 $P < 0.05.$

tabulated for each of the 20 verbal samples in Table 1.

The actual scoring of the verbal samples was done by us working together, not independently, and all final scores were obtained by consensus. No test was made of reliability of scoring by two independent professionally trained judges using this method of thematic analysis in this particular experiment. The correlation between independent judges scoring according to a similar, but more difficult and complicated, system of verbal analysis was found to be 0.86.² In the present study, a test was made of the reliability of a nonprofessional person's scores on 20 verbal samples, using the Schedule, and the correlation with the scores by consensus of two psychiatrists was 0.70. These findings will be discussed later.

Several assumptions were made in this part of our method. The first was that the frequency of occurrence of specific content categories in the five-minute verbal samples was proportional to the intensity of the patient's emotional state. The second was that the categories were of equivalent importance and were of equivalent relevance to her psychologic state, and therefore were additive. The third was that positively and negatively scored categories canceled each other out. We were skeptical that these mathematical assumptions represented exactly the complicated processes of human problem solving, thinking, and feeling. But without prior clear-cut evidence to tell us how to deal with our data, without a mathematical model of cognition and emotion, we believed that these

were reasonable approximations to use in order to validate the hypothesis, if a relationship did exist between the patient's psychologic and physiologic states.

We were now able to rank the 20 verbal samples, by our thematic scores, in order of those supposedly indicating the least intense to those indicating the most intense conflict, from highest plus to highest minus (corrected) scores.

These rankings of what we presumed to be relative intensity of psychologic conflict and distress could now be tested for their predictive value in discriminating those periods of time when the patient's total Streptococcus counts were relatively high and relatively low. The 20 rankings of degree of specific psychologic conflict were compared with the rankings of the relative percentage of Streptococcus colonies from the patient's throat.

The bacteriologist's reports were kept sealed until the conclusion of the psychologic evaluations. Spearman's formula for rank-difference correlation was used to determine the correlations between the psychologic and the bacteriologic data.

Results

The rankings of the relative intensity of the psychologic conflict during the 20 periods when compared with the rankings of the relative percentages of Streptococci are also shown in Table 1. This Table shows that when Category 6 ("blocking, difficulty

in performing, giving") was excluded from among our criteria, a significant correlation was found ($r=0.41$; $P<0.05$ on a one-tailed test) between our psychologic and bacteriologic ratings. But when this category was included, there was no significant correlation ($r=0.20$). It will be recalled that this category had been considered a priori of questionable pertinence to the intensity of the psychologic cluster we were trying to estimate, and our original hypothesis was that a significant association between the two complex variables (bacteriologic and psychologic) would be found either with or without the counting of this category of references.

We attempted further confirmation of the results by a further test. Twelve samples of verbal data produced by the same patient during the preliminary study, but which had not been used to formulate our hypothesis, were used to retest the hypothesis. These were tape-recorded interviews of various lengths, running 10 to 60 minutes. The first 500 words of each interview were utilized for thematic analysis. These were scored in the same manner as our 20 five-minute verbal samples, but in this instance the category "blocking, etc." was not included. All other criteria in the thematic coding system were used. They were scored without knowledge of the bacteriologic results (Table 2). Again, a significant association ($r=0.51$; $P<0.05$) was found.

TABLE 2.—Further Validation of a Quantitative Relationship Between Psychologic and Bacteriologic Variables

Interview No.	Streptococcal Colonies		Thematically Coded Interviews	
	Per Cent	Rank	Score	Rank
1	87	11	-2.40	7
2	70	5.5	-1.00	3
3	90	12	-4.00	11.5
4	85	9.5	-2.80	9.5
5	80	7.5	-1.40	4
6	80	7.5	-4.00	11.5
7	70	5.5	-0.20	2
8	54	1	-1.80	5
9	55	2.5	+1.80	1
10	85	2.5	-2.40	7
11	85	9.5	-2.40	7
12	67	4	-2.80	9.5

$\Sigma d = 138$
 $r = 0.51$
 $P < 0.05$

The scores of the 20 five-minute samples (without the "blocking, etc." category) were then combined with the 12 samples from the original data, and the total 32 samples were ranked and compared with the Streptococcus count rankings. An over-all correlation of 0.46 was found, which gives even further support to the hypothesis that our method of verbal-behavior analysis provides valid predictive data of a quantitative type.

Before the bacteriologic data were opened, an impressionistic evaluation was attempted, without using our system of counting categories of references, of the relative intensity of conflict revealed in each five-minute verbal sample. It was found to be quite difficult to arrange the 20 verbal samples in the order of that sample showing the most to that showing the least specific emotional conflict and distress, for we found it very taxing to keep in mind the many criteria necessary to arrive at a decision. Nevertheless, we persisted with this impressionistic method of estimating relative intensity of psychologic conflict. (As many investigators know, this method is the principal one available to clinicians in such clinical research activities with a patient.) We (L. A. G. and S. K.) came to a consensus about our impressionistic rankings. When we compared these impressionistic rankings of relative intensity of psychologic conflict with the bacteriologic rankings, we found, however, that the correlation was not significant ($r=0.11$) and that this method of evaluation was of no predictive value in this type of experimental problem.

We were curious to determine whether our assumption had some validity, that verbal references by our patient to the involvement of a person other than the self in any one of the content categories (except Category 6 §) gave pertinent information about our patient's own subjective state of conflict. For this reason, we recalculated on the total 32 verbal samples the rankings of the intensity of the patient's psychologic conflict, counting, on the one

§ From Schedule.

hand, only those references in which other subjects (*b*)§ and unspecified subjects (*c*)§ were involved and, on the other hand, counting separately only those references in which feelings or activities pertaining to the self (*a*)§ were involved. The rankings of our patient's psychologic state based on these two separate breakdowns were compared with the bacteriologic rankings. It was found that both references to persons other than the self having experiences falling within our categories ($r=0.39$) and references only in terms of the self as the experiencing object ($r=0.26$) were important and necessary factors in assessing our patient's relative degree of distressing conflict. Neither type of verbal reference alone was sufficient to account for the significant psychophysiology correlation we had found ($r=0.46$) when both types of verbal references were used in the calculation.

Comment

In this study, we have attempted to test the validity of a method of estimating the variations in the intensity of a subject's psychologic conflict or state. The psychologic state we have measured in the present study is not a single conflict but, rather, a cluster of conflicts and reactions stemming from a basic psychologic conflict of unsatisfied dependency. It may appear that we have not specifically demonstrated that our experimental method of verbal analysis is a direct measure of mental events, for we have succeeded in showing only that we could predict, beyond the limits of chance probability, the percentage variations in streptococcal colonies cultured from our subject's throat. That our experimental method measures mental experience is an inference. The significant correlations of our verbal-content scores with the bacteriologic data lend support to the inference that we are measuring not only a behavioral variable, i. e., frequencies of referential categories in speech, but also a psychologic variable.

§ From Schedule.

Another experiment we have done has direct bearing on this point. In this experiment, using a generally similar system of scoring and counting, as in the present method but employing somewhat different categories,² we more directly attempted to compare our experimental method of assessing the psychologic status of patients with the evaluations obtained by another set of psychologic criteria. In that study we were interested in the speech patterns of schizophrenic patients. We sought to determine whether we could assess the varying degree of personal disorganization and social alienation in eight different chronic male schizophrenes by analyzing 5 to 21 three-minute verbal samples elicited from each patient in a standardized way. The set of criteria with which we compared our experimental procedure was the combined, independent ratings by two psychiatrists who had access to all data charted in the patient's daily records, including interview notes or other material by attending psychiatrists and other physicians, nurses' notes, and comments by social workers and occupational and recreational therapists. The over-all result of this study was that counting the frequency of occurrence of certain typical features in small samples of the verbal communications of a schizophrenic person provided a valid and reliable quantitative estimate of the relative severity of his disorder from time to time. We conclude from our experiment using schizophrenic patients and from the present study that our experimental method of verbal analysis is of predictive value in measuring degree of personal disorganization and social alienation, and certain physiologic changes within a patient, and, if we cannot directly demonstrate that it measures psychologic status, we can show it does measure a variety of correlates of such.

Our findings suggest that, within limits, what a person feels and how a person is trying to solve personal conflicts (many of which may be below the level of awareness) are not indicated simply by what a person

says but by how often he says something. Furthermore, even though one ignores the issue of how a person says one thing and concentrates on what he says over a period of minutes, one may well be able to ascertain the intensity and type of emotional conflict that is being experienced. The evidence for this latter statement lies in the fact that our scores in this experimental method were based only on typewritten copies of speech. Vocal intonation, accent, pitch, and intensity were cues that were not used in this process of evaluation, and, though we could have listened to the tape recordings of each verbal sample, we did not do so. We realize that these aspects of speaking are very important in the communication of human emotion and conflict, but apparently content analysis alone gives quite reliable information—within the limits of our studies—about the varying mental states of a person.

Some readers at this point may pose the question as to whether the correlation of psychologic and bacteriologic variables in our one patient was due to the patient's feeling symptomatically worse and more disgruntled, the more bacteriologic infection she had. But at no time during the studies with this patient was there any evidence that she had an infection, an invasion of the oropharyngeal mucous membranes by streptococcal bacteria. No signs occurred of inflammation of the throat or any associated temperature rise or leukocytosis. The changes in the bacteriologic flora of her throat were variations occurring without signs of local infection. They were probably secondary to pH and other variations in the oropharyngeal secretions, as well as being due to variations in the vascularity of this area, without there being any decisive diminution in the effectiveness of the pharyngeal mucosa as a physical and immunologic barrier to frank infection. We conjecture that there must be, somewhere in the central nervous system, an integrating center that makes it possible for the "culture medium" of the throat to vary directly

in its physical properties with the state of distress versus satisfaction of the total organism. We think it is likely that humoral mechanisms, such as the activity level of the hypothalamic-pituitary-adrenocortical axis, play a part in this regulatory balance. But we can offer no more definite facts or theories on the intermediating variables responsible for the observed psychophysiologic relationship.

Another point worthy of attention is that the five-minute samples of speech produced by our patient for this study were all spoken in response to the standardized instructions of a technical assistant. This assistant was the only person present in the room when the patient's speech was tape-recorded, and the assistant had only this role with the patient, no frankly administrative, psychotherapeutic, medical, or other one. The introduction of a technician in obtaining the speech samples, instead of her medical physician or psychiatrist, did not interfere in any discernible way with the predictive capacity of the scores obtained from these verbal samples. We think it is an important discovery to learn that a procedure as sensitive as this method appears to be can be administered by a person who is not professionally trained. The fact appears to be that under certain circumstances it is not necessary to consider the problem of who elicits the verbal behavior in order to make it useful and valid as data. In this sense, it is possible that speech itself is the royal road to psychodynamic assessment. The problem is, as Freud demonstrated with dreams, to find the way to decode speech in order to give information about the workings of conscious and unconscious psychologic conflicts.

We have just begun to determine, once a system of decoding has been established, whether a nonprofessionally trained person can code and score speech samples with high reliability. On the only test of this question that we have so far carried out, a technician's scoring of 20 verbal samples showed a correlation of 0.70 as compared

with the scorings by consensus of two psychiatrists. It is likely that with practice a higher correlation can be attained.

Finally, the discussion of our findings cannot be brought to a close without acknowledging the application of psychoanalytic theory and concepts to the design of our experimental method of verbal analysis. The instructions used in the standardized method of eliciting the verbal samples read: "This is a study of speaking and conversational habits. Upon a signal from me I would like you to start telling me about any interesting or dramatic personal life experiences you have had. Once you have started I will be here listening to you but I would prefer not to reply to any questions you may feel like asking me until the five-minute period is over. Do you have any questions you would like to ask me now before we start? Well, then, you may start." These instructions were designed to simulate the psychoanalytic interview. The lack of verbal responsiveness of the examiner during the period the subject is speaking, plus a conscious attempt on the part of the examiner to keep at a minimum any nonverbal cues that might indicate his reactions to the subject, tend to give the examiner and the total situation the quality of a "blank screen" on which the patient projects some part of the gamut of his reactions to any vaguely similar life situations. Presumably what the patient talks about at any one session depends in part on what psychologic conflicts and feelings are being most prominently experienced at that time, i. e., what feelings and conflicts are most highly cathected and focal. This psychologic state determines how the subject perceives the experimental situation and of what remote or recent past events he is reminded. The standardized and stereotyped nature of the situation in which the verbal samples are elicited minimizes the examiner as a variable in influencing the patient's subjective state and speech (i. e., countertransference effects are kept relatively constant) and leaves the subject's re-

actions (i. e., transference effects) as the predominant variable.

Our finding that a subject's verbal references to other persons being involved in some pertinent emotional experiences tends to indicate that a similar emotional state is occurring in the speaker, perhaps a wish or counterwish, is in concordance with the psychoanalytic concept of "displacement" as a psychologic mechanism of coping with anxiety.

The scoring of relevant content, regardless of whether it was expressed in the form of past, present, or future tenses, as conditional probabilities, or in the optative, is an application of the concept of primary process thinking to the evaluation of verbal activity. As will be recalled, primary process thinking is that which is characteristic of the immature part of the personality, thinking which is characterized by condensation, displacement, and symbolization. In primary process thinking a sense of time does not occur, and past, present, and future are all one. The use of these and other psychoanalytic concepts is basic in the construction and design of our method of verbal-behavior analysis.

Summary and Conclusions

This paper is a report of one application of an experimental method designed to provide quantitative estimates of the relative severity of a specific cluster of psychologic conflicts in one person over a large number of periods of observation. The procedure involves collecting electronic tape recordings of five-minute samples of speech from the subject, under standardized instructions, and doing frequency counts of relevant content categories occurring per unit of communication (grammatical clause) in the verbal samples: Some of the content categories are a priori given a positive weighting (+1) and some a negative weighting (-1). The algebraic sum of these plus and minus scores per verbal sample, divided by the total number of words spoken in the verbal sample ($\times 100$) is used to provide a

quantitative estimate of the intensity of psychologic conflicts at any one time.

This verbal-analysis method of assessing intensity of psychologic conflict was used in a study attempting to validate a previously observed association in a 32-year-old woman between the intensity of a psychologic state and the percentage of streptococcal colonies cultured from her throat. In an initial 20 trials, a significant correlation ($r=0.41$) was demonstrated between the psychologic and the bacteriologic variables. The comparison of scores obtained from another 12 verbal samples and throat cultures again revealed a significant correlation ($r=0.51$). Combining these 32 rankings of psychologic state and comparing them with the bacteriologic rankings gave an over-all correlation of 0.45.

Verbal references by the patient to persons other than the self experiencing relevant content were demonstrated to be important indicators of the subjective experience of the patient.

The five-minute samples of speech necessary to make estimates of intensity of psychologic conflict may be obtained by a technician or secretary without apparently interfering with the predictive capacity of the scores obtained by their analysis.

Theoretical and practical considerations of this experimental method of verbal analysis are discussed.

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Chlorpromazine Used with an Intensive Occupational Therapy Program

A Controlled Study

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Introduction

Chronic schizophrenia accounts for approximately two out of three long-stay mental hospital patients in Great Britain.⁴ Interest in the therapeutic approach to this enormous problem has been stimulated by the development of the tranquilizing agents, particularly chlorpromazine; and there is now an extensive literature reporting the use of this drug in chronic schizophrenia. The consensus appears to be that chlorpromazine is a useful treatment for this group of patients, especially when aggressiveness, overactivity, or psychotic tension is a prominent symptom, though even with this most widely used tranquilizer there have been isolated controlled studies with completely negative results.⁷

At the same time, partly arising from the evidence of numerous drug trials, there has been a renewed awareness that chronic mental hospital patients benefit from environmental changes, especially where increased activity and enhanced social interaction between patients and staff result.^{1,6,9} Robin¹¹ concluded that occupational therapy had a quieting effect on aggressive patients, superior to that produced by tranquilizing agents, and suggested that there might be "a current tendency to think in terms of the physical or pharmacological treatments in the handling of psychotic patients and to overlook the value of more conservative measures."

The fact that the use of drugs in mental hospital chronic wards is likely to produce a far-reaching social and psychological impact on the therapeutic setting makes critical evaluation of the specific drug effect of tranquilizers particularly difficult. It is this type of extrapharmacological factor, particularly variations of staff attitudes and expectations from one hospital to another, that Sabshin and Ramot¹² have suggested may account for the apparent incompatibility of strongly positive and negative reports of trials with the same drug.

From a consideration of the literature, it would seem that a therapeutic program which combined the use of a tranquilizing drug with increased occupational and social activities should be more effective with chronic schizophrenics than either treatment alone. Cowden et al.³ reported that chlorpromazine as an adjunct to group psychotherapy gave slightly superior results to chlorpromazine alone in chronic schizophrenia, but we have been unable to find any controlled study in which chlorpromazine has been used as an adjunct to an energetic resocialization program.

This paper describes such an investigation: an attempt to isolate the specific drug effect of a widely used tranquilizer, chlorpromazine, when used to treat a group of chronic schizophrenics in the setting of an energetic program of increased occupational and social activities. In this way we intended to throw light on the relative size of the contributions of the drug and the environment to the over-all effect of the total therapeutic program.

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Method

General Description.—A number of female chronic schizophrenics took part in a 12-week program of increased occupational and social activities. Matched groups of these patients received, in addition, chlorpromazine or inert tablets throughout the special program, and for a further 12-week period after it had ceased. It was hypothesized that the patients receiving chlorpromazine would (a) show and (b) sustain an improvement in behavior significantly greater than would those not receiving the active drug.

Selection and Matching of Experimental Population.—Suitable patients from a closed ward, who had not previously received treatment with chlorpromazine, were assessed on a number of variables: age, duration of illness, intelligence, and aptitude for occupational therapy. From these patients one of us (P. G.) selected two groups, matching them as closely as possible on the variables. The pharmacist decided at random which group would receive chlorpromazine and which inert tablets, and only she had this information at any time.

In order to have adequate numbers for statistical treatment of the results and yet groups small enough for individual attention in occupational therapy, the whole experimental program was replicated. The final population consisted of a first sample, A (14 patients), and a second sample, B (16 patients). Patients were paired as closely as possible within each sample so that, if any patient had to discontinue the program, her "pair" could also be omitted. In addition, great care was taken to eliminate other possible sources of bias in the construction of the matched groups. Thus, two more disturbed patients, and any only recently transferred to the ward, or having received other types of treatment, for instance ECT, were allocated equally to the two groups. Three pairs were

lost: one due to death from unassociated causes; two due to major side-effects, mentioned later. Data on the remaining 24 patients are tabulated in Table 1.

As will be seen, there were no significant differences between the two groups on the matched variables; nor was there any significant difference in the levels of their behavior, as shown in their initial mean Behavioral Rating Scale scores, although this criterion was not used in the matching process. The occupational therapy (OT) aptitude score was a simple rating made by the OT staff on the basis of their knowledge of the patients' initial capabilities. Its purpose was to ensure that the two groups were equally accessible to what would be one of the most important features of the therapeutic program.

Ward Environment.—The experimental ward was classified as a closed ward for 50 disturbed and deteriorated chronic psychotic women. There had been a treatment program on the ward for at least 18 months, with maintenance electroconvulsive therapy, chlorpromazine, and, more recently, some organized occupational therapy, and a weekly social for the less disturbed patients; improvements in ward atmosphere had already occurred. Our population was therefore probably less deteriorated and disturbed than many reported in the literature. The majority of our patients dressed and fed themselves with little or no supervision, and incontinence was infrequent; acts of physical aggression or destructiveness were also uncommon. However, they were nearly all unoccupied unless under constant supervision, showed irritability or overactivity in phases, and sustained virtually no social relationships on the ward.

Treatment Program.—Special Program of Social and Occupational activities: This was designed by the Head Occupational Therapist to be as varied as possible. In addition to individually supervised basketry, sewing, and soft-toy making, there were

TABLE 1.—Population Data

	Experimental		Control		t *	Total	
	Mean	S. D.	Mean	S. D.		Mean	S. D.
Age	49.33	10.04	50.17	11.39			
Duration of illness	19.17	12.19	20.08	11.41	0.18	49.75	10.74
OT aptitude	5.08	2.46	4.17	2.03	0.18	19.62	11.82
ABRS Ward rating 1	36.33	11.06	45.54	17.30	0.94	4.62	2.32
ABRS OT rating 1	42.50	9.11	43.50	9.24	1.475	40.92	15.20
					0.265	43.00	9.19
	Mean	Range	Mean	Range	U †	Mean	Range
Psychological Tests							
Information	4.64	0-15	4.64	0-13	60	4.64	0-15
Vocabulary	22.09	1-45	16.73	1-44	52	19.41	1-45
Mazes	8.09	0-31	7.55	0-21	54.5	7.82	0-31
No. of patients previously receiving							
ECT	7		9		--		16
Insulin coma	2		1		--		3

* The t-value should be 1.717 or more to show significance at the 0.1 level of confidence.

† The nonparametric U-statistic was used because of the grossly abnormal distributions of scores. ¹⁴ U should be 34 or less to show significance at the 0.1 level of confidence.

sessions of art therapy; music therapy, including a percussion band, eurythmics, physical exercises, and games; instruction in make-up and in letter writing, and a mixed social club with music and dancing. Within the framework of the program, there was harnessed a great deal of individual attention and encouragement from the occupational therapy and nursing staff, who all seemed positive in their attitude toward the experiment. As far as possible, one senior nurse on each shift was allocated to the group, accompanying them to all their activities, and the Head Occupational Therapist worked with the patients individually for at least one session every day. The OT staff were instructed to give no extra attention either to those progressing most quickly or to those lagging behind. At the end of 12 weeks the patients were returned to their usual routine, which included some less intensive OT in a different room. The second sample started their special program within a few weeks of the end of the first 12-week program.

Drug Regime: Chlorpromazine tablets or sugar-coated placebo tablets in divided doses, amounting to 150 mg. daily, were given from individually labeled bottles. It was realized that much higher doses have been recommended by some workers, but our previous experience with this moderate dosage had been favorable, and we were particularly anxious to avoid the daytime somnolence so often accompanying a higher dosage. In terms of subjective experience, it could be said that the actual taking of tablets was probably a relatively insignificant feature of the total therapeutic program experienced by the patients. This drug regime was continued unchanged for a further 12 weeks after the special program had ceased and until the final behavior ratings were made.

Measurement of Improvement.—Behavioral Rating Scale: Since it was hypothesized that improvement would be in behavior and ward adjustment, the main measure used was the behavioral rating scale. The Albany Behavioural Rating Scale (ABRS), devised by Shatin and Freed¹⁸ and consisting of 100 items, was chosen for this purpose. This scale had been developed in connection with a resocialization program similar to our own; adequate standardization data on chronic psychotics had been described; the wide range of social behavior in our group was adequately covered, and, with the elimination of very few of the items, the scale was scored without difficulty by the Ward Sister and the Head Occupational Therapist. The scale as we finally used it consisted of a simple check list of 97 items, e. g., "... will always reply if you make some remark to her," which were scored as true or false in their application to a particular patient; A patient's final score was the number of items checked in a healthy direction, so that high scores indicated greater normality

than low scores. Any improvement in observed behavior should therefore lead to an increased ABRS score.

Each patient was rated independently by the Ward Sister and the Head Occupational Therapist. This ensured that the observations covered two different social settings and were made by people who were differently trained. The observers also differed in respect of their roles in the therapeutic situation and had different expectations about the results of the program: The Ward Sister had considerable faith in a drug which was familiar to her, whereas the Head Occupational Therapist expected that the effect of the intensive OT program would overshadow any drug effects. The subjective biases of our raters were therefore opposite in direction, and it was thought that a combination of ward and OT ratings would give a more accurate assessment of the patient's actual state than either rating separately.

Ratings were made at the end of the 1st, 6th, 12th, and 24th weeks of the experiment. For the final rating the patients were brought together again and observed for one week in the setting of the special program. Improvement throughout the total population would be measured by the difference between the scores on the initial ratings and those made at the 12th and 24th weeks.

For a comparison of the improvements of the chlorpromazine and placebo groups, two General Improvement Scores were calculated for each patient, as follows: The sum of the initial ward and OT rating scores was subtracted from the sum of the corresponding scores at three months (GIS3) and at six months (GIS6).

OT Improvement Rating: At the end of the special program the various therapists rated the patients on a simple scale ranging from "slightly worse" to "much improved" (1 to 4). No patient was found to deserve the rating "much worse." The sum of a patient's ratings on individual activities was her final score on the OT Improvement Rating.

Cognitive Tests: A vocabulary test, a simple information-orientation test, and a simple perceptual maze test were carried out by all but the two most disturbed patients during the week before the special program began, and repeated during the week following its cessation. No real change was expected on these tests, which were included, rather, for their possible predictive value.

Results

A. Behavioral Rating Score Changes.—

1. A comparison of the initial mean scores on the ABRS with the mean scores at three and six months shows that considerable

increases occurred throughout the total group of 24 patients. The mean score changes at both three and six months, whether the ward, OT, or combined ratings were used, proved to be highly significant at the 0.0005 level (a one-tailed test was used, since the direction of change had been predicted). If the ABRs score changes are accepted as a criterion of behavioral improvement, it is clear that a marked improvement in observed behavior took place throughout the total group.

2. The increase took place almost entirely in the three months during which the patients were subjected to the special program and was approximately equally distributed between the first and the second half of this period. The differences in the total-group mean scores between the three- and the six-month ratings were small and nonsignificant. This suggests that the improvement in observed behavior was stabilized after three months, but interesting internal differences were noted in the reaction of the different subgroups of patients to the withdrawal of the special program: These are discussed later.

3. The mean scores of the chlorpromazine and placebo groups on GIS3 were 58.83 and 41.58, respectively. This difference of 17.25 is significant at the 0.01 level of confidence, using the method outlined by Lindquist⁵ for estimating the standard error of the difference between the means of matched groups and allowing for a multiple correlation of 0.551 between the matched variables and the criterion. The superiority of the chlorpromazine group over the control group on GIS6 was 17.67, significant at the 0.05 level.

4. Before these differences could be accepted as due to a drug effect, it was essential to exclude any subjective bias that would preferentially influence the ratings of the chlorpromazine group. Successful identification of those patients receiving the active drug as a result of evident side-effects appeared to be the main possible source of bias. Therefore at the end of the

experiment both raters were asked to "guess" the composition of the chlorpromazine group. The following percentages of successful guesses were scored:

	Sample A N=6	Sample B N=6
Ward Sister	83.3%	66.7%
Head OT	66.7%	50.0%

From discussion, it appeared that one of the minor side-effects led to the Ward Sister's correctly guessing all but one of the six Sample A patients receiving chlorpromazine: This was photosensitivity, and the patients were noticed, during a period of summer sunshine, to have what appeared to be a marked sunburn of the face. In Sample B, treated in the early winter months, this side-effect did not occur.

Such slight bias as might result from the two 66.7% successful guesses (i. e., guessing one more patient out of six than would occur by pure chance) would tend to be canceled out in view of the difference in subjective bias of the Ward Sister and the Head Occupational Therapist; but clearly the Ward Sister's ratings on the six patients in Sample A, apart from her initial rating, could not be accepted as free from subjective bias.

5. Revised Improvement Scores were therefore devised which eliminated the potentially biased ratings. For Sample B patients the combined ward and OT ratings were used as described for GIS3 and GIS6, but for Sample A patients the sum of the initial ward and OT ratings was subtracted from the doubled OT rating score at three months (RIS3) or at six months (RIS6). Both the chlorpromazine and the placebo group were equally affected by this reorganization, and no potentially biased scores were included.

The differences in mean RIS between the chlorpromazine and the placebo group were 16.17 at three months, significant at the 0.02 level, and 15.50 at six months, significant at the 0.05 level. A biserial correlation run between taking chlorpromazine and improvement showed a significant relation-

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TABLE 2.—ABRS Mean Score Changes

Ward Ratings	Experimental			Control			Total Group
	Sample A	Sample B	Total	Sample A	Sample B	Total	Total
1	32.33	40.33	36.33	39.17	51.83	45.50	40.92
2	49.67 *	52.17	50.92 *	44.33	58.50	51.42	51.17 *
3	60.83 *	67.67	64.25 *	55.00	63.33	59.17	61.71 *
4	62.17 *	65.17	63.67 *	59.83	57.17	58.50	61.08 *
OT Ratings							
1	37.00	48.00	42.50	41.17	45.83	43.50	43.00
2	50.17	54.83	52.50	47.00	60.50	53.75	53.12
3	60.00	66.83	63.42	56.33	66.50	61.42	62.42
4	59.83	66.83	63.33	61.83	60.17	61.00	62.17
RIS3	50.67	46.17	48.42	32.33	32.17	32.25	40.33
RIS6	60.33	53.67	57.00	53.33	29.67	41.50	49.25

* Contaminated ratings: omitted from RIS3 and RIS6.

ship at three months of 0.481, which dropped slightly to 0.333 (nonsignificant) at six months.

These results show a definite superiority of the chlorpromazine patients over the controls in their behavioral response to the experiment and suggest that they were aided by the drug. The effect of the drug was not striking as compared with the over-all improvement of the total group, but this estimate of its effect is, of course, free from any of the possible defects which are said to occur with successive ratings on a behavior rating scale of the type used in this study.¹ We can, therefore, state definitely that the first part of our original hypothesis was confirmed; as regards the second part our results were equivocal.

6. As can be seen from Table 2, the subgroups differed in their reaction to the cessation of the stimulus of the special program. The control patients in Sample A continued to improve throughout the second three-month period, while the control patients in Sample B declined during the equivalent period to about their six-week level on both the ward and the OT ratings. Throughout the corresponding periods the mean scores of the chlorpromazine patients in both Sample A and Sample B showed no significant deviation in either direction.

The number of patients is too small to justify definite conclusions on the reason for these differences. However, the most obvious explanation of the difference in reaction of the control patients in the two samples is that Sample A patients may have

been affected by the special program taking place on the ward with Sample B patients; when Sample B patients finished their special program, it was to all intents and purposes the end of the experiment, and this may have resulted in a lessening of nursing enthusiasm. The chlorpromazine patients seem both to have reached their peak improvement more quickly and to have been more stable in maintaining the level reached.

7. Analysis of the areas of behavioral change on the subscales within the ABRS failed to show that the superiority of the chlorpromazine group could be explained on the basis of a drug effect acting on any single area of behavior. In both drug and control groups the areas of greatest improvement were reaction to environment, self-care, cooperation, and socialization, in that order.

8. Comparison at six months of the four most improved and the four least improved patients out of the total group revealed the following contrasts: The four most improved patients had a mean age of 34 years 9 months, and a mean duration of illness of 5 years; the four least improved patients had a mean age of 52 years 3 months, and a mean duration of illness of 23 years.

To discover the prognostic value of the criteria on which the patients were assessed, correlations with the Revised Improvement Scores at three and six months were calculated. These are shown in Table 3.

It is clear that in this group of patients duration of illness is the most important single prognostic factor, having a significant

TABLE 3.—Correlates of Improvement

	Total Group (N=24)		Chlorpromazine Group Only (N=12)	
	3 Mo. RIS	6 Mo. RIS	3 Mo. RIS	6 Mo. RIS
Age	-0.425 *	-0.460 *	-0.441	-0.409
Duration of illness	-0.417 *	-0.514 †	-0.537	-0.641 *
OT aptitude	0.367	0.312	0.166	0.288
ABRS ward rating 1	-0.188	-0.324	-0.333	-0.313
ABRS: OT rating 1	0.186	0.244	0.113	0.218
Information 1	0.276	0.332	0.269	0.528
Vocabulary 1	0.313	0.316	0.053	0.213
Mazes 1	0.209	0.535 †	0.206	0.670 *
Having chlorpromazine RIS 3 mo.	0.481 *	0.333	--	--
	--	0.825 †	--	0.858 †

* Significant at 0.05 level.

† Significant at 0.01 level.

negative correlation with improvement. Age is also an important prognostic factor, but in this group of patients the relationship of age and duration of illness is so close ($r=0.735$) that only one of these variables need be taken into account. The best predictive battery of factors was found to be initial ward rating, OT trainability, and either age (multiple $r=0.554$ with RIS3) or duration of illness (multiple $r=0.702$ with RIS6).

Of the intellectual tests, an adaptation of the Porteus Mazes⁸ gave the best prediction of improvement at six months, but these results could not be included in the predictive battery because of their grossly abnormal distribution.*

9. Four of the patients (17%) were "much improved" by the usual clinical criteria and reached a level where their discharge from hospital could be recommended. These four patients were also among the top five on the RIS6 and were equally divided between the chlorpromazine and the placebo groups. Two of the patients, one in each group, have successfully been on discharge for several months, but the other two are still awaiting the solution of purely social problems that are preventing their discharge. Two patients, both in the con-

trol group, showed a slight behavioral deterioration in their RIS at six months. Between these two extremes, of fitness for discharge and deterioration, the degrees of improvement were approximately normally distributed throughout the total group. Several months after the end of the experiment the ward staff maintains that the patients remain more friendly and interested in occupational and social activities. The ward itself, previously classified as "closed refractory," has now been opened.

After the experiment, when the administration of all tablets ceased, the ward staff reported relapses in 8 of the 12 patients who had had chlorpromazine: The administration of the drug was restarted and appeared to check the relapses. No sudden relapses were reported in the patients who had been taking placebo tablets, but five of these patients were started on chlorpromazine, and three showed an apparent good response; in one of these patients, who had shown very little improvement during the special program, the response was very marked.

B. OT Improvement Score.—Only a slight and nonsignificant difference was found between the chlorpromazine and the placebo group using the OT Improvement Score, based on the subjective ratings of the individual therapists. The mean ratings for the two groups were 6.42 and 5.42, respectively. It seems possible that the ratings used involved too coarse a scale of measurement to pick up the slight differences between the groups which were reflected in the more objective and detailed ABRs.

C. Cognitive Tests.—Intercorrelations of the cognitive tests ranged from 0.55 to 0.70, suggesting that some general intellectual function was being tapped. No significant change on retesting on any of these tests occurred in either the chlorpromazine or the placebo group. This was as expected and suggests that neither the drug nor the therapeutic program produced any improvement in the level of intellectual functioning.

* Spearman's Rank Order Correlation and the Mann-Whitney *U*-test of significance of the difference between two groups were used for the cognitive-test results because of their abnormal distributions. All the other correlations were Product-Moment.

D. Side-Effects.—Two major complications occurred: one case of jaundice, and one, more serious, of agranulocytosis, which, fortunately, recovered on appropriate treatment. This incidence of serious side-effects is much higher than could have been anticipated from published reports, but it serves as a reminder that treatment with chlorpromazine carries a small, but definite, risk.

Minor side-effects were ubiquitous, but, except for photosensitivity, which was mentioned above, these appeared to have had little bearing on the results, and we avoided focusing nursing attention on recording them in detail.

Comment

Our findings indicate that both chlorpromazine and the total environmental effect of the occupational program contributed significantly to the changes observed in the patients. Of the two treatments, the therapeutic program was clearly the more important. In fact, our results suggest that the chlorpromazine had a greater effect on the speed than on the level of improvement.

Although we have no evidence on the point, it seems possible from a consideration of the literature that if our population had been more grossly overactive and aggressive a more marked drug effect might have been shown. Similarly, a higher dosage of chlorpromazine might have led to a greater improvement in some of the patients.

It seemed that the actual effect of the drug on our patients was to enhance their over-all response to the therapeutic program. Perhaps the most obvious explanation of this would be that the drug made the patients more accessible to the other therapeutic influences by controlling their psychotic tension and overactivity, but analysis of the subscales of the ABRs provides no evidence to confirm this.

The occurrence of easily observed side-effects represents a serious difficulty in planning controlled investigation of tran-

quilizing drugs. That nurses may identify the patients receiving the active drug with a high percentage of success, and the implications of this, are now well recognized²; but many authors still either ignore this difficulty altogether or fail to make due allowances for possible bias in the interpretation of their results. Our study shows that, although it may sometimes be impossible to eliminate the potential bias, its extent can be fairly accurately measured and means found of freeing the results from its influence.

Age and great length of illness seemed to militate against any patient showing great improvement in response to either drug or environmental influences; and this would support the contention that efforts should be concentrated on resocializing chronic schizophrenics before the terminal stages of institutionalization have been reached.

Although the abilities measured by the cognitive tests appeared to be related to one another, only the Maze test showed any marked association with behavioral improvement. This test was originally included because of its reported positive relationship to social improvement⁸ and apparent usefulness with senile deteriorated patients.¹⁵ Our results are consistent with the previous findings and suggest that this type of test might with advantage be used more frequently to study the chronic or deteriorated patient, particularly when resocialization programs are contemplated.

We confirm the frequently made observation that far-reaching social effects on the patients' environment may accompany, and outlast, a research of this sort. The nursing staff involved in the investigation have gained in an increased awareness of the importance of good nurse-patient relationships and of environmental influences. They seem less inclined to rely exclusively on physical treatments and drugs as the only methods of improving the health of their patients.

The considerable mean score improvements on the ABRS are probably best regarded as operational measures of the changed pattern of social interaction between the patients and the raters: Objective improvements in the patients' behavior contribute to the rating scale changes but are not the only factor to which they can be ascribed. The raters themselves tend to change toward more accepting, tolerant attitudes toward patients, and these, in turn, evoke more friendly responses from the patients.

It is impossible to draw any conclusions from this study as to the relative values of the various activities of the special program. It is also clear that it would be quite impracticable within the limits of mental hospital staffing to maintain such an intensive program for long periods with all chronic schizophrenics. The present study, however, does raise the question as to whether intensive occupational programs with small groups of chronic patients for limited periods may not be a more effective therapeutic contribution from the Occupational Therapy department than attempts to keep as many chronic patients as possible occupied with routine tasks or craft work.

In this research chlorpromazine and the special program appeared to act synergistically. However, the interrelation of environmental and drug effects on chronic schizophrenics may not be as simple as this. Rashkis and Smarr¹⁰ have recently published the surprising finding, in a series of chronic schizophrenics, that when a period of environmental change was followed by a period of drug administration there appeared to be an inverse relationship between the amount of improvement resulting from the environmental change and that resulting from the drugs. They therefore questioned the possibility of a trial with environmental change for each patient before drugs are prescribed. This finding has not been cross validated, but a possible criticism of the present study is that our groups were not matched for "reactivity to environmental

change," a criterion which could only have been assessed by a preliminary trial. It might be argued that our results could be explained without invoking a drug effect, by supposing that our chlorpromazine group contained more patients strongly reactive to environmental change than did our control group. This can hardly be sustained, however, when it is remembered that the chlorpromazine group showed a marked lack of reactivity, as compared with the placebo group, to the environmental change involved in the cessation of the therapeutic program.

There would seem to be some need for further research into the nature of the relationship between the responsiveness of chronic schizophrenics to environmental changes, on the one hand, and pharmacological and physical treatments, on the other. We should not be justified in making broad generalizations on the basis of this small-scale investigation, but our results tend to support a growing clinical impression that, at least in chronic schizophrenia, chlorpromazine is better used not as the sole treatment but as an adjunct to a therapeutic program of environmental and social encouragement.

Summary and Conclusions

An investigation is reported in which the effect of chlorpromazine is assessed when used as an adjunct to a special program of occupational and social activities in the treatment of chronic schizophrenia. The findings may be summarized as follows:

1. Matched groups of female chronic schizophrenics were given either chlorpromazine or placebo tablets in addition to an energetic resocialization program, lasting 12 weeks. Great care was taken to control all variables in treatment except the drug itself. The tablets were continued for a further period of 12 weeks after the end of the resocialization program.
2. Results suggested that a considerable behavioral improvement took place throughout the total group during the 12 weeks of

the special program. During the second period of 12 weeks there was marked variability of behavioral response: Reasons for this variability are tentatively offered.

3. The patients also receiving chlorpromazine showed a slight but statistically significant superiority in their improvement over the control patients after three months. Their superiority was still significant but was less marked after six months.

4. A source of possible bias in the identification of experimental group patients due to photosensitivity was discovered. Its measurement, and the elimination of its influence from the results, are described.

5. Age and duration of illness were the most important factors in predicting behavioral improvement, both showing significant negative correlations. A simple Maze test also seemed to have long-term prognostic value.

These findings are briefly discussed and the following conclusions put forward:

1. Chlorpromazine is a useful adjunct to a therapeutic program with chronic schizophrenics.

2. Used in this way, chlorpromazine appears to have a greater effect on the speed than on the final level of improvement.

3. A short intensive occupational and social program is capable of producing considerable behavioral improvement in chronic schizophrenic patients.

4. Efforts should be concentrated on resocializing chronic patients before the terminal stages of institutionalization have been reached.

This study was initiated on the suggestion of the Head Occupational Therapist, Mrs. F. Fransella; the enthusiastic cooperation of Ward Sisters M. Marchant and E. O'Loughlin and the members of the Occupational Therapy Department made the research possible; Dr. R. N. Davis, the Medical Officer in charge of the ward, helped in selecting suitable patients, and the Pharmacist, Miss B. Peterson supervised the dispensing of the drug and the placebo tablets, and, finally, Dr. J. H. Watkin, Physician Superintendent, Horton Hospital, gave encouragement and support in carrying out the study and permitted the results to be published.

Horton Hospital (Dr. Waters).

Grygier—Waters

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Dynamic Aspects of Occupational Therapy

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A feature disturbing to occupational therapists in many mental institutions is their low prestige within the therapeutic team. Should a grading of the ancillary services according to their value for the therapeutic process be attempted, psychiatrists and patients alike would probably rank the nursing profession highest, social workers second, and occupational therapists lowest. Reasons for this low ranking, as far as psychiatrists are concerned, may be (a) lack of knowledge and insufficient appreciation of the services rendered by occupational therapists, and (b) an appropriate, justifiable response to the inadequate contribution of this ancillary service to the therapeutic process.

In what follows, psychiatric occupational therapy will be submitted to a critical analysis, and some suggestions will be advanced as to how its scope could be enlarged. The paper will deal with (1) some historical considerations, (2) the training and orientation of occupational therapists, (3) a field survey of occupational therapy, and (4) an attempt at reconceptualizing occupational therapy.

I. Some Historical Considerations

A glance at the history of occupational therapy shows that its application to the mentally ill long antedated its application to patients suffering from any other disorders and that their employment in the so-

called hospital industries preceded any other forms of occupational therapy.

Impetus to the movement, strange as it may appear, was given by prison reforms early in the 19th century. It was indeed a great advance in penology when prisoners were allowed to work. Yet the privilege to work, which may well have boosted the morale of the prisoners, shades so easily into exploitation of cheap labor for the sake of economy and into hard labor imposed as a means of punishment.

Attempts followed "to cheer up the mentally ill and to make them forget their troubles" by keeping them busy and by offering them recreation and amusement.

Occupational therapy in its present form came into being during the First World War, when activities which had proved of value for the physically disabled, such as weaving and basketry, were rather indiscriminately taken over for the treatment of the mentally ill. Craft teachers were employed, and formal instruction in music, painting, drawing, or other arts and crafts was provided. The development of skills and the "beauty and perfection" of the finished product, rather than the care of the patient, were then the primary objectives of many occupational therapists and have remained the primary objectives of some of them ever since.

This brief excursion into the history of occupational therapy shows (1) that hospital industries may be an incentive toward improvement but may also be abused as cheap labor (in the interest of hospital economy) and as hard labor (inflicted by a vindictive society); (2) that, rather naively, attempts have been made to cheer up the mentally ill and to make them forget their troubles, and (3) that, mistakenly, at

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some time and in some quarters, occupational therapy for the mentally ill has been concentrated on production or the product rather than the patient.

II. Training and Orientation of Occupational Therapists

Perusal of the textbooks used for the training of occupational therapists indicates that occupational therapists in general, and those entrusted with the care of the mentally ill especially, are inadequately trained in psychiatry. It is often stated that understanding of the principles of psychiatry and the basic problems of the patient is essential for the work of occupational therapists; but, in fact, with few exceptions, only a bare outline of the descriptive features of common mental illnesses is given in most textbooks used for training.

Occupational therapy came into use on empirical grounds. Writers on the subject take it for granted (*a*) that work and recreation per se have a remedial effect on the mentally ill, (*b*) that occupational therapy facilitates the effect of other therapeutic measures, and (*c*) that the media used are well suited to bring about the desired effects. But none of these hypotheses has been submitted to rigorously designed research techniques. In fact, as occupational therapy is usually given in combination with other therapeutic measures, it is, of necessity, unknown which does which and whether the arts and crafts employed have the effects attributed and expected.

There is a lamentable lack of adequate theory of psychiatric occupational therapy. Statements, such as the following, are made in textbooks used for students:

The aim of the occupational therapists is to find some work which will stimulate the patients' interest in something outside themselves . . . We must try and replace morbid, unhealthy ideas by normal healthy ones . . . Idleness hastens physical and mental deterioration . . . A chic uniform, important work and the group relationships are stimulating.

Other writers espouse and practice in their application of occupational therapy what might be described as a symptomatic

or vectorial approach to mental illness. They concentrate their efforts on such isolated symptoms as incontinence of bladder and bowel, social withdrawal, and difficulties in handling aggressiveness, which, by means of habituation, reeducation, resocialization, and social remotivation, they hope to rectify. All these measures have in common a learning process, a disregard for unconscious mental processes, and an appeal to an ego impoverished in function by the inroads of mental illness.

It is a moot point whether and to what extent the symptomatic approach and the measures adopted in accordance with it, directed as they are toward removal of isolated symptoms, fundamentally affect the disease process as such. The most that tentatively can be said is that they seem to counteract the regressing effect of prolonged hospitalization; that they seem to improve manageability; that they lessen the sense of futility and uselessness so common in chronic patients, and that they facilitate the transition from the world of the sick to the world of the healthy in patients approaching a condition which allows their discharge.

III. A Partial Field Survey of Psychiatric Occupational Therapy

The impression gained that the training of psychiatric occupational therapists is unsatisfactory and that the theoretical foundations of occupational therapy, as practiced at present, leave much to be desired, was confirmed by a field survey carried out by us.¹

The aim of the survey was to obtain information about the views on and attitudes toward occupational therapy of patients, occupational therapists, and psychiatrists.

All in all, 50 patients, 22 psychiatrists, and 21 occupational therapists were interviewed at 15 major psychiatric centers in Canada and parts of the northeastern United States. A majority of the occupational therapists interviewed were heads of the departments or teachers in schools of occupational therapy.

(a) *Patients*.—Two-thirds of the patients were psychotic; one-third, psychoneurotic. The majority of the patients showed much interest in occupational therapy and felt that it brought them relief. However, they were perplexed about the purpose of the activities offered them, and many of them had a feeling that occupational therapy had little to do with their treatment, since "the doctor was not there." Typical statements were these: "It helps pass time. . . . It keeps you busy. . . . It occupies your mind."

(b) *Occupational Therapists*.—The interviews with the occupational therapists were based on a questionnaire especially designed for the study. The data obtained could be analyzed under four general headings: the meaning and function of occupational therapy; the role of media; the theoretical framework of occupational therapy; the occupational therapist-psychiatrist relationship.

Meaning and Function: The response to the request to define the function of their field of activity indicated that occupational therapy by all but one was conceived of as a means to direct attention from fantasy and inner preoccupation in order to produce a "normal" atmosphere for a "pleasant occupation" and to socialize. In brief, occupational therapy was conceptualized as an instrument of ego strengthening through two main mechanisms of defense, namely, repression and suppression. Overlooked were the facts that the inability of the patient's ego system to control the emergence of impulses may be responsible for his incapacity to live "normally," that his retreat from reality may be due to his anxiety arising from social contacts, and that the preponderance of fantasies and restitutional activities may be the sole manner of adaptation remaining for the patient. The problem of interaction with other patients and with the therapist was hardly ever considered.

Role of Media: The function of the media in general was identified with that of occupational therapy itself, i. e., to divert,

to normalize, and to facilitate the relief of excess energy. No or little regard was given to the symbolic significance of the created or chosen object as an unconscious means of projecting intolerable impulses, painful feelings, and objectionable attitudes, or to the possibility of using created or chosen objects as a means of uncovering drives, defenses, and transference phenomena.

Theoretical Framework: All the occupational therapists interviewed agreed that there was no adequate theory of psychiatric occupational therapy, i. e., a coherent system with adequate linking concepts constructed to explain the phenomena observed and to serve as a guide for activities to be beneficially employed. This vacuum seems to be due to the predominant orientation of heads of schools of occupational therapy toward physical medicine; to the adherence of psychiatric occupational therapists to descriptive psychiatry, with neglect of present psychopathological theories (i. e., to a time lag in development and orientation), and to a lack of interest on the part of psychiatrists in occupational therapy and failure to realize its potentialities. The points made explain why cooperation between psychiatrists and occupational therapists is frequently lacking.

Occupational Therapist-Psychiatrist Relationship: Out of the 21 occupational therapists interviewed, 17 indicated that this relationship was unsatisfactory. By cooperation they meant the writing of prescriptions (indicating the history and phenomenology) by the doctor and his occasional visit to the department to see what the patients "were doing." Statements such as these were common: "The doctor does not know much about occupational therapy. . . . The doctor is only interested in seeing that the patient is doing something. . . . The doctor fails to convey to the patient that occupational therapy can be part of his treatment."

(c) *Psychiatrists*.—What do psychiatrists know about occupational therapy, and what is their attitude toward it?

Our survey revealed that the level of the psychiatrist's interest in and attitude toward occupational therapy depended on his orientation toward psychopathology and his knowledge of and insight into group dynamics.

Psychiatrists with little understanding of psychodynamics used occupational therapy freely, yet with the avowed purpose of breaking the monotony of the long and weary hours between somatic treatment procedures and meals. In a setting of this kind the job of an occupational therapist is disheartening and her prestige is low. Psychiatrists with more training in and understanding of psychodynamics had, more or less, formed a personal conception of occupational therapy, if and whenever they used it. Their main formulation included expression, canalization, and sublimation of aggressive drives. The psychoanalysts interviewed, with one exception, did not use occupational therapy at all.

IV. Tentative Reconceptualization of Occupational Therapy

It is our view that the practical value of occupational therapy could be greatly enhanced if it could be made theoretically meaningful in terms of psychodynamic concepts. Its present usage with emphasis on resocialization, on the one hand, and the teaching of crafts and skills, on the other, disregards the dynamic significance of the offered and created object. We feel that the dynamic formulation of occupational therapy should make use of the three related theories of instincts, of mental structure, and of object-relations. For the sake of brevity, we shall omit a detailed discussion and shall mention only three concepts derived from the above theories, namely, sublimation, projection, and gratification. We have used the last two concepts in developing two particular therapeutic procedures.

(a) *Sublimation*.—The main objective of traditional occupational and recreational therapy is sublimation, i. e., discharge of

infantile drives in an inhibited, desexualized form.

However, it should be borne in mind that the capacity to sublimate has been impaired in, or lost by, the mentally ill. It is therefore illogical to assume that activities which require the capacity to sublimate, offered to these patients in the hospital environment, will enable them to do what they had been unable to do outside. From this it follows that the objects and activities offered must be in keeping with the regressive needs of the patients.

(b) *Projection*.—Beyond this, unstructured material, such as Plasticine, can be used for the creation of objects which—analogue to a dream—may serve as a screen on which fantasies may be projected, with their associated drives and defenses erected against them.

Based on these projective mechanisms, Azima and Azima designed and developed a treatment procedure which they called "projective group therapy."² Over a prolonged period, groups of patients, mainly psychoneurotics, have been asked at each treatment session at first to create what comes to their mind (free creation period) and then to say what comes to their mind in connection with their creations (free association period). Psychoanalytic interpretations were given. For details of our method, we refer to our publications on this subject. Suffice it to state that four years of experience with it have shown us that the created objects have the following functions and effects:

1. They have a facilitatory effect on the uncovering of defenses, drives, and transference relationships.
2. They may regressively revive early projective mechanisms.
3. They act by their continuous presence as powerful stimuli to the uncovering of unconscious mental processes in the patient and other members of the group.

* This procedure was originally called "analytic group art therapy."²

4. They may serve as a means of (1) discharge of needs and (2) reorganization of needs.

(c) *Gratification*.—The third general concept, that of gratification of infantile needs, is taken as a useful theoretical and pragmatic test for occupational therapy because it can be seen as the logical consequence of the two hypotheses: (1) that a partial libidinal and aggressive regression to certain fixation points is a comprehensible dynamic feature of all psychopathological states, and (2) that these fixation points and the regressive trends toward them are genetically initiated by frustration through inadequate gratification of basic object needs. The concept of gratification finds its logical position here, and it will bring two complementary hypotheses: (1) that by fostering regression to and beyond these fixation points and by gratification of originally frustrated needs, the fixation point may be abandoned and a progression may ensue; and (2) that this gratification should be fostered by offering of appropriate primitive objects, in a correspondent set of relationships. It is felt that the latter two hypotheses, particularly the last, are applicable to occupational therapy and posit meaningfully the object (created, chosen, or offered) as the point of emphasis of the procedure.

We have applied these considerations to the treatment of chronic schizophrenic patients, and we have thought it useful to call this treatment "object relations therapy."⁴⁻⁶ The main feature of the procedure was the offering of primitive media, such as mud, brown clay, baby bottle, etc., with the aim of encouragement of regression and gratification, followed by gradual introduction of more structural objects. The object-relation setting was that of a mother-child relation, and the fostered direction of regression was from anal to oral. Once again reference must be made to our published work.

Conclusions

In the introduction to this paper the question is raised whether the low prestige of occupational therapists in many mental institutions is due to the insufficient appreciation of their contribution or to insufficiency of their contribution. Both viewpoints are probably valid. It has been shown that the training of occupational therapists in psychiatry is inadequate, that an adequate rationale for the application of this therapy is lacking, and that research is urgently needed regarding a theoretical basis for its procedure. The view is expressed that the practical value of occupational therapy could be enhanced if it could be made meaningful in terms of psychodynamic concepts. A tentative attempt is made to reconceptualize its application. A plea for postgraduate training of occupational therapists in dynamic psychiatry may be made.

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Analeptic Action of Lysergic Acid Diethylamide (LSD-25) Against Pentobarbital

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Adventitious findings in this laboratory indicate that lysergic acid diethylamide (LSD-25) protects cats against the toxic effects of large doses of pentobarbital. One hundred forty cats have survived inordinate amounts of pentobarbital at the termination of experiments in which LSD-25 solution was given systemically.

Gastaut,¹³ Bradley,^{3,4} and others^{6,8,14,18} provide electrophysiological evidence that LSD-25 antagonizes the action of anesthetic doses of barbiturates. In these studies the actions of both drugs on the frontal cortex and on the reticular formation were investigated. There appear to be no reports, however, of the extent to which LSD might inhibit or reverse lethal effects of larger doses of barbiturates. It seemed worth while, therefore, to investigate in greater detail this protective property of LSD.

Under the conditions of the present studies, LSD-25 safely and effectively reversed respiratory and central nervous system depression induced in cats by lethal doses of pentobarbital. What is more, LSD-25 was more effective than picrotoxin or pentylenetetrazol U. S. P. (Metrazol) in this regard.

Material and Procedures

METHOD I.—Ability of Drugs to Prevent Suppression of Respiratory and Cortical Activity by High Doses of Pentobarbital.—One hundred eighty-six cats anesthetized with 42 mg. of pentobarbital sodium per kilogram intraperitoneally were used in this part of the study. (Sixty milligrams per

kilogram kills a cat within 30 minutes of intraperitoneal injection.) The animal was immobilized in a Horsley-Clarke apparatus, and one femoral vein was exposed. The parietal cortex was exposed, and platinum electrodes were placed in contact with the surface. Silver electrodes were placed under the skin of the abdomen and of the thorax. All electrodes were led to a Grass electroencephalograph. In this way cortical, respiratory, and cardiac activities were recorded. Forty minutes after the original anesthetizing dose of pentobarbital, one of the following drugs was given intraperitoneally:

To 101 cats, LSD-25 solution, 50 μ g. per kilogram of body weight; to 7 cats, brom-LSD (2-brom-d-lysergic acid diethylamide), 50 μ g. per kilogram of body weight; to 17 cats, picrotoxin, 1.5 mg. per kilogram; to 7 cats, pentylenetetrazol, 0.05 gm. per kilogram; to 14 cats, crystalline LSD-25,* 50 μ g. per kilogram, and to 7 cats, no drug other than pentobarbital. Fifteen minutes after the test drug was injected, two-thirds of an anesthetizing dose of pentobarbital (called the first lethal dose) was administered intraperitoneally. The LSD series is large because at first we suspected that our pentobarbital was weaker than labeled. We used three different supplies of pentobarbital. To 13 animals still surviving because of a previous dose of LSD solution, repeated lethal doses of pentobarbital were given at 10-minute intervals until all 13 cats were dead, as confirmed by EEG, respiratory, and cardiac records.

Thirty-nine cats were given 50 μ g. of LSD-25 per kilogram, followed 15 minutes later by a single injection of a double anesthetizing dose of pentobarbital. No surgery was done on these cats.

METHOD II.—Ability of Drugs to Reverse Respiratory and Central Nervous System Depression Induced by Lethal Doses of Pentobarbital.—Eighty-three cats were prepared for recordings as in the first group of tests. Forty minutes after the initial anesthetizing dose of pentobarbital, all cats were given a lethal dose of the drug. The lethal dose was a second dose two-thirds of the

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*Previous studies on the ocular properties of LSD-25 indicated that crystalline LSD-25 was not as active as the solution.

Efficacy of Various Analeptic Agents Against Lethal Doses of Pentobarbital

	Lethal Dose Pento- barbital	No. Survived	% Survival
No. of Cats Treated with LSD-25 Solution			
Before	140	140	100
After	42	33	78.6
No. of Cats Treated with Picrotoxin			
Before	17	17	100
After	29	11	37.8
No. of Cats Treated with Pentylene-tetrazol			
Before	7	7	100
After	9	0	0
No. of Cats Treated with Brom-LSD			
Before	7	1	14.3
After	6	0	0
No. of Cats Treated with LSD-25 Crystals			
Before	14	1	7.2
After	6	0	0

anesthetizing dose. Recordings were watched. When cortical activity became markedly depressed and respirations ceased but the heart beat remained, the test drugs were given in the following manner:

In this series, 42 cats received LSD-25 solution, 10 μ g/kg. I. V., injected very slowly, and 50 μ g/kg. intraperitoneally; 29 cats received picrotoxin 0.5 mg/kg. I. V. in two doses, five minutes apart and 1.5 mg/kg. intraperitoneally; 6 cats received crystalline LSD-25 on the same dose schedule as that on which other cats received LSD-25 solution; 6 cats received brom-LSD also on the same dose schedule as LSD-25.

In Method II the EEG tracings were watched until restoration of normal sleep EEG activity, until death, or, in some cases 8 to 16 hours after administration of the test drugs (until no further change could be expected).

Results

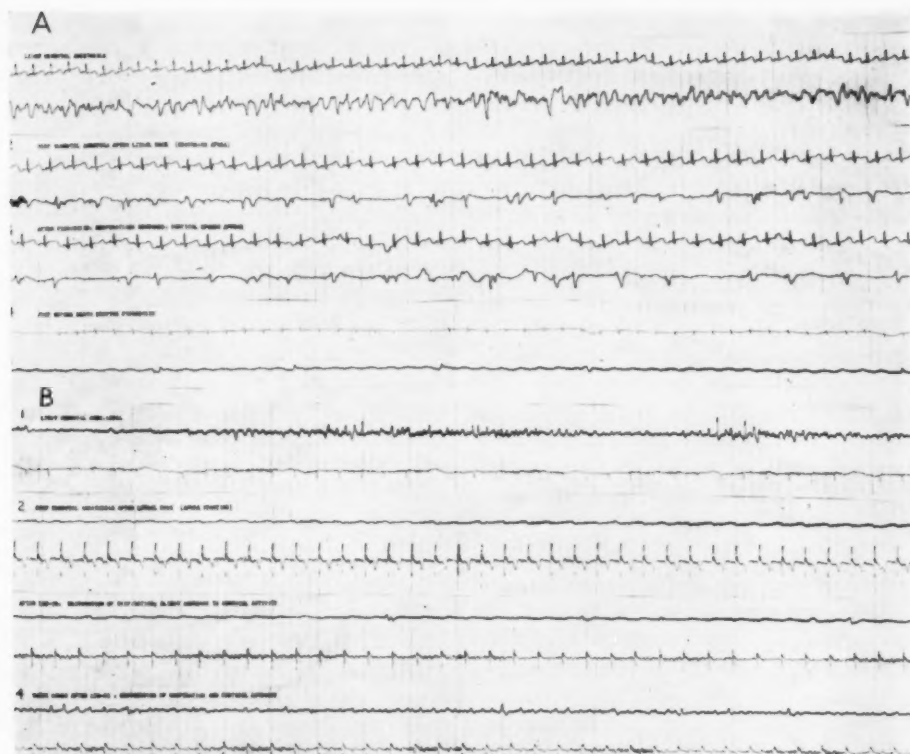
I. All cats not given a test drug died 6 to 10 minutes after receiving the first lethal dose of pentobarbital sodium. Crystalline LSD-25 did not change this course of events. Cats receiving brom-LSD before the lethal dose of pentobarbital showed marked suppression of the EEG and respirations after pentobarbital and died within two hours after the lethal dose. All the cats receiving pentylene-tetrazol, picrotoxin, or LSD-25 solution survived at least six hours after one lethal dose of pentobarbital and showed no suppression of the EEG and very slight suppression of respiratory rate. On

the other hand, two lethal doses killed all the cats receiving pentylene-tetrazol or picrotoxin but not those protected by LSD-25. The 101 LSD cats with exposed parietal cortex survived two lethal doses at least eight hours. They showed some suppression of EEG and respiration. These tracings returned to normal sleep-spindle-type records within 6 to 14 hours. It required three lethal doses of pentobarbital given at once or at 10-minute intervals to kill the cats protected by LSD solution. The 39 cats spared surgery and given two lethal doses of pentobarbital after LSD all recovered completely and were used in subsequent experiments.

II. All the cats given a lethal dose of pentobarbital showed marked suppression of the EEG in 4 minutes, of respiratory depth in 6 minutes, and of cardiac action in 10 minutes. Brom-LSD or crystalline LSD did not change this course of events. Picrotoxin restored respiration and some EEG bursts of spikes for a few minutes and kept 62.2% of the cats alive for 20 to 40 minutes and 37.8% for more than 6 hours. LSD solution restored respiration depth and rate in two minutes after intravenous administration. There were minimal signs of restored EEG activity until 60 to 80 minutes after LSD was given. At that time, EEG activity was like normal sleep records, or nearly so. Seventy-eight per cent of these cats lived for at least eight hours, and then two lethal doses were required to terminate the experiment.

Several precautions were taken during these experiments and are worthy of note. The animals were never moved after injection of a lethal dose of pentobarbital. Whenever an animal was carried, however carefully, it promptly died. These cats are not included in this series. The animals were kept warm, and all handling was gentle. If the animals lost a great deal of blood during surgery, they were discarded from this series.

The discrepancy in action between LSD-25 solution and crystalline LSD should be



(A) In each pair of tracings the upper one is the EKG, with slow oscillations from movement of the abdomen during respiration; the lower tracing is of potentials from the surface of the parietal cortex. 1, recordings after anesthesia with pentobarbital; 2, depression of cortical potentials and cessation of respiration six minutes after a lethal dose of pentobarbital; 3, cortical spikes and restored respiration two minutes after injection of picrotoxin intravenously and intraperitoneally; 4, irreversible changes leading to death: tachycardia, absence of cortical activity, apnea.

(B) In each pair of tracings the lower one is the EKG, with an electromyogram of respiratory muscles superimposed; the upper tracing is of potentials from the surface of the parietal cortex. 1, recordings after anesthesia, showing sleep spindles; 2, depression of cortical activity and apnea (LSD-25 was given intravenously and intraperitoneally given at this point); 3, restored respiration but not much change in cortical potentials 20 minutes later; 4, restored cortical potentials three hours later. This animal survived eight hours and was killed by a double anesthetizing dose of pentobarbital.

Time marking 0.4 second. Amplitude calibration is not contributory.

emphasized. In studying the ocular properties of LSD,^{1,2} we found that the crystalline form induced the same respiratory and cardiac stimulation that LSD solution did, but the crystalline form did not induce similar ocular results. Therefore, the success of LSD-25 solution in the present study should be attributed not to respiratory and cardiac stimulation alone but, rather, to some special property yet to be identified.

Apter

Comment

The pentobarbital-induced EEG changes reported by Clark and Ward,⁷ Brazier,⁸ and Finesinger and Brazier¹⁰ helped orient the depth of anesthesia in the present study. Sleep spindles were prominent in the parietal cortex before the lethal dose of pentobarbital was given. As the lethal dose took effect, random slow activity, then long quiescent periods with a few bursts of spikes were recognized. Six minutes after the

lethal dose the bursts of spikes disappeared and respirations ceased. At this point the analeptic drugs were given intravenously. All the successful drugs (LSD, picrotoxin, pentylenetetrazol) started respiration within a few seconds. Only pentylenetetrazol and picrotoxin initiated cortical spikes,²⁰ however. Each intravenous dose of an analeptic drug was supported by an intraperitoneal dose. In about 10 minutes the effect of the sustained supply of analeptic drug appeared in the EEG as low-amplitude spikes. All the pentylenetetrazol- and 62% of the picrotoxin-supported cats eventually died. Of the LSD-supported cats, 78.6% eventually recovered normal sleep spindles. The LSD cats that were not exposed to surgery survived this hazardous experience and were used in subsequent experiments.

These studies give no information concerning the basis for an antagonism between LSD-25 and pentobarbital. The work of others, however, provides clues. French et al.¹¹ find that barbiturates inhibit synaptic transmission in the reticular formation. Bradley and Key⁴ report that LSD-25 increases the amplitude of spontaneous potentials in the peripheral (but not in the cortical) afferents to the reticular formation. Moreover, peripheral stimulation is one method employed in preventing collapse from large doses of barbiturates in humans¹² and is based on physiological evidence.¹⁵⁻¹⁷ These facts suggest that LSD-25 may be capable of increasing the input from the periphery into the reticular formation. In this way LSD could help the organism to overcome resistance built up by pentobarbital at the synapses in this region. If this resistance¹⁷ is the cause of death from large doses of pentobarbital, then overcoming the resistance would prevent death. Until more is known concerning the actions of pentobarbital and of LSD, further theorizing is merely speculation.

The contribution of the present study is in the demonstration that LSD safely and effectively overcomes cortical and respiratory inhibition induced in cats by lethal doses of

pentobarbital. This fact can be useful to workers who find an animal succumbing to an overdose of pentobarbital during an experiment. It may also prove useful in cases of acute pentobarbital intoxication in human subjects when heroic measures are called for to protect the subject from the toxicosis. The best manner in which to use LSD under such circumstances cannot be deduced from the present report.

It should be emphasized that the doses of LSD used in this study are harmless to vital functions in both anesthetized and unanesthetized cats.^{9,10} On the other hand, the doses of picrotoxin necessary to reverse pentobarbital intoxication are convulsive in unanesthetized animals and produce cortical spikes indicating a near-convulsive state in anesthetized animals.

Summary

The relative value of LSD-25 solution, LSD-25 crystals, pentylenetetrazol U. S. P. (Metrazol), picrotoxin, and brom-LSD to prevent and to reverse pentobarbital (Nembutal) intoxication was investigated in 269 cats.

LSD-25 solution proved more effective in safe doses than did picrotoxin, pentylenetetrazol, and brom-LSD (in that order) in preventing death from subsequent lethal doses of pentobarbital. Crystalline LSD had no protective effect.

LSD-25 solution was more effective than picrotoxin in safe doses in reversing cortical suppression and cessation of respiration induced by previously administered lethal doses of pentobarbital. Crystalline LSD and brom-LSD had no such effect under the conditions of this experiment.

The doses of LSD-25 solution necessary to prevent and to reverse pentobarbital death are harmless to vital functions in both unanesthetized and anesthetized cats, whereas the doses of picrotoxin necessary to reverse pentobarbital toxicosis are convulsive or subconvulsive even in anesthetized cats.

The relevance of this protective property of LSD-25 to the therapy of barbiturate

intoxication in humans requires further exploration.

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Constancy of the Funkenstein Test

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In the course of a study of the effect of electroshock treatment on various systems in the body, Funkenstein tests were routinely performed two weeks after the completion of a course of treatment and repeated two weeks later. It was observed that, although patients often fell into a different grouping on the second test, their clinical condition, measured by gross behavior, often did not reveal any significant change. The question arose regarding the degree to which changes normally occurred in the Funkenstein grouping. To find the answer to this question, the constancy of the Funkenstein test was studied by repeating the test every two or three days in a group of patients over a period of two to four weeks.

Although there is no formal report of experimental work on the constancy of the Funkenstein test, observations on this subject were reported in the discussion of the symposium on tranquilizing drugs¹ held in 1955. Dr. L. J. West tested the reliability of the Funkenstein test by subjecting a group of 15 patients to a series of 12 tests, which were performed every other day. He found variation in the results of the test from day to day but did not describe the extent of the variation. Dr. Frank J. Ayd Jr. reported that he tested patients several times during the same day and observed variation in the Funkenstein test within a period of four hours. He observed, however, that any one given patient would fall in the same group most of the time. He

was impressed with the reliability of the test after having administered 1000 tests to 400 patients. Our work was undertaken without knowledge of these studies.

Since the test is considered a measure of the status of the autonomic nervous system, the results might be expected to vary with the normal day-to-day fluctuation in the emotional states of the subjects. On the other hand, if the test is to be a reliable prognostic tool for predicting the effectiveness of shock therapy, it should be expected to remain reasonably constant despite day-to-day variations in patients' emotional states. The test would be of less value if, for example, its results varied with the mood swings that are seen in manic-depressive disorders. In order to exclude this variable as much as possible, regressed chronic schizophrenic patients who showed little in the way of day-to-day change in behavior were employed as subjects and a record was kept of all gross changes in each patient's mental status during the period of testing.

The test was given as described by Funkenstein and associates.² In the interest of greater accuracy the same person (a registered nurse) administered all the tests. During the course of the study the subjects received no sedatives or tranquilizing drugs. There was no change in their routine day-to-day activities as hospitalized patients on the continued treatment service, except for the administration of the test. None of the subjects showed any significant change in mental status throughout the period in which they were being tested.

Thirteen chronic schizophrenic patients were employed as subjects. Their average length of illness was 10 years, and their average length of hospitalization at the Brentwood Veterans' Administration Cen-

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From the Department of Psychiatry, University of California School of Medicine at Los Angeles, and the Veterans' Administration Center (Brentwood Neuropsychiatric Hospital). This study was made possible by a grant from the Mental Hygiene Foundation of Los Angeles.

CONSTANCY OF FUNKENSTEIN TEST

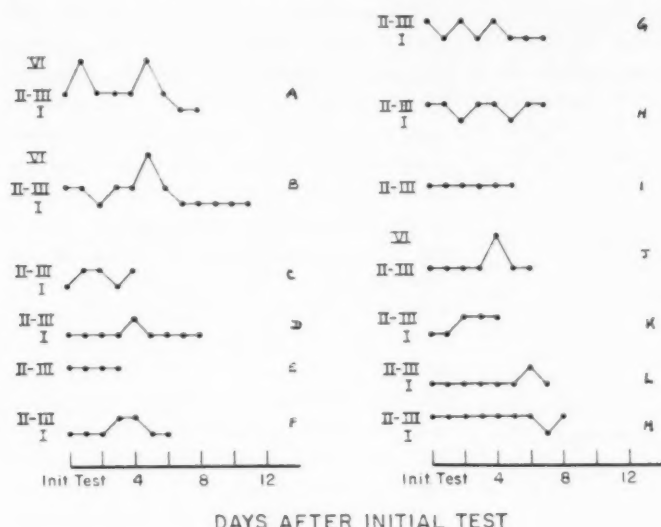


Fig. 1.—Variation in Funkenstein group on repeated testing.

ter was approximately 5 years. All of the patients had been hospitalized elsewhere prior to admission. Eleven of the thirteen patients had received electroconvulsive treatment in the past, some having had several courses. For the most part, the patients were withdrawn and manneristic. They showed varying degrees of uncommunicativeness and were actively hallucinating or deluded. They constituted a regressed group of patients who had not responded to active treatment in the past and who were regarded as having poor prognoses. A total of 97 tests were given. The results are shown in Figure 1.

Of the 13 patients, 2 showed no change in group in repeated testing. Eight of the thirteen patients showed only minor changes, which consisted of varying degrees of fluctuation between Group I and Group II-III. The blood pressure curves of these groups are quite similar, and differentiation was often difficult. According to Funkenstein, the expected improvement rate with ECT is low in both these groups (9% in Group I and 35% in Group II-III). In only three instances (Cases A, B, and J) did more significant variation occur. An example is illustrated in Figure 2. Clinically, these three patients did not differ from the

others. All three had had electroconvulsive treatment in the past with no better response than the others.

In any given patient, although the grouping might change with repeated testing, the shape of the blood pressure curve produced

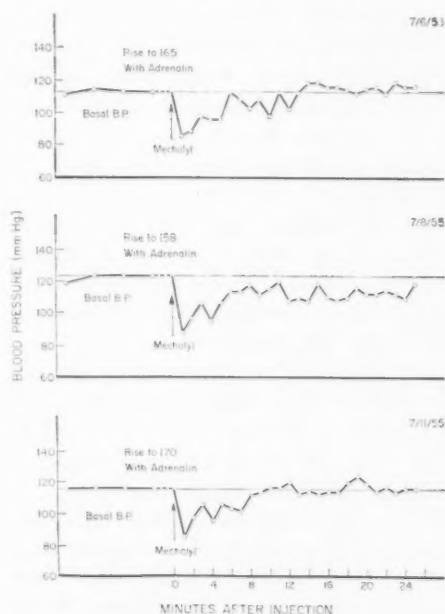


Fig. 2.—Variation in Funkenstein test pattern in Subject B on repeated testing.

by methacholine (Mecholyl) injection tended to remain the same. In most instances the change in grouping was the result of a change in the base line. This finding was observed by Weckowicz,³ who tested a group of 20 patients with various psychiatric diagnoses morning and evening in an attempt to learn whether there was a diurnal variation in the results of the test that corresponded to the level of the activity of the sleep-wakefulness centers in the hypothalamus or its vicinity. He found a change in type of reaction in 5 of the 20 patients. Three who reacted with a rise of blood pressure in the morning reacted with a fall of blood pressure in the evening. Two others showed just the reverse. Weckowicz commented on the individual patterns of reaction (i.e., the type of curve) and the tendency of each patient's pattern to remain unchanged.

Geocarls and Kooiker⁴ performed single Funkenstein tests on a group of 25 patients with chronic schizophrenia who had been continuously hospitalized for at least five years and found that all of the patients fell in Groups I and II-III, with one exception, who fell in Group V. On initial testing, our cases, which were clinically similar, all fell in Groups I and II-III.

In any given patient there was no consistent correlation between the base line blood pressure and the prognosis as indicated by the grouping on the Funkenstein test. In some instances the basal blood pressure was lower when the grouping was VI than when the grouping was II. However, when the base line blood pressures of all tests falling in Group I, Group II-III, and Group VI were averaged, it was found that the Group I average was lowest (103.25 mm. Hg) and the Group VI average was highest (132.7 mm. Hg). The Group II-III average occupied an intermediate position (112.17 mm. Hg). This suggests some over-all relationship between basal blood pressure and prognosis, as indicated by the Funkenstein test.

These blood pressure findings are consistent with Funkenstein's hypothesis that the better prognosis seen in these patients in his Groups VI and VII is related to a state of increased sympathetic tension associated with an active parasympathetic system that gives rise to the sustained drop in blood pressure in these patients following the administration of methacholine. The tendency of these patients to have an initially higher blood pressure may indicate some continued appropriate autonomic cardiovascular response to psychic stress. In contrast, those with low blood pressure and increased parasympathetic tension to begin with may not be reacting to stress appropriately, perhaps because of the extent of their psychotic withdrawal from reality. Stimuli which would normally result in a stimulation of sympathetic centers in the hypothalamus (as has been suggested by Gellhorn) no longer do so to the same degree, perhaps because of lack of reinforcement or actual central distortion of the stimulus.

The observation that some variation does occur in repeated Funkenstein tests is of interest. It may be that those few patients with chronic schizophrenic reactions who on occasion change from Group I or Groups II-III to Group VI possess residuals of more appropriate autonomic responsivity to stress. Although they may not be distinguishable from observations of their gross behavior from other chronic patients, more refined methods of examination may reveal that they are different. They did not show any greater amount of overt anxiety or responsiveness in interviews. Their reaction to a noxious painful stimulus was no different, and they did not differ as a group in their response to an experimental situation that was designed to provoke anxiety. Although having poor prognoses to usual modes of treatment, including electroconvulsive treatment, they might be more responsive to intensive individual treatment.

CONSTANCY OF FUNKENSTEIN TEST

These hypotheses would seem worthy of testing.

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Oculomotor and Postural Patterns in Schizophrenic Children

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The persistence of primitive postural and righting reflexes in schizophrenic children has been stressed by Lauretta Bender and her associates.¹⁻³ They claim that such reflexes, particularly the tonic neck reflex, are retained in these children far beyond the normal age and are a manifestation of a disturbance in the maturational processes. The studies by Silver⁴ and Teicher⁵ of the postural and righting responses of schizophrenic children support these concepts. These children had no signs of neurologic disease as measured by standard techniques. They did show motor disturbances when examined in special ways, e.g., whirling when the head was passively rotated, a phenomenon also found in children with organic brain disease.⁶

Although Bender¹⁻³ stresses the role of tonic neck reflexes in the motility patterns of schizophrenic children, and Schilder⁷ emphasized the importance of vestibular function in psychosis, there has been no survey of the vestibular functions in such children. Nor have their oculomotor patterns been studied in detail, although these movements may be part of the righting reflex and are closely associated with vestibular function. The present study was, therefore, undertaken as an attempt to assay these functions in a group of early-school-aged schizophrenic children.

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Department of Neurology, the Mount Sinai Hospital, and the Henry Ittelson Center for Child Research. This study was supported, in part, by a grant from the Ittelson Family Foundation.

Subjects

The experimental group consisted of 15 schizophrenic children in residential treatment. They ranged from 7 to 9 years of age. Seven children, diagnosed as having nonschizophrenic behavior disorders, served as clinical controls. They were of comparable age and lived in the same treatment center as the schizophrenic group. The normal control group comprised nine children, aged 3 to 10 years. Six of these were randomly selected from the pediatric service of the Mount Sinai Hospital, and three were nonhospitalized school children.

Procedure

Oculomotor Examination.—Three types of oculomotor function were examined: requested eye movements, optokinetic nystagmus, and the reflex reaction to a sudden exposure of a small light in a dark room. The requested movements were of three types: (a) schematic (subject asked to look to his left or right, or up or down); (b) command (subject asked to fix a target in extrapersonal space), and (c) pursuit (subject asked to follow a moving target). Convergence and divergence were also examined. All of these movements were recorded by measuring the corneoretinal potential with the aid of an electroencephalogram according to a standard technique.⁸

The apparatus employed for optokinetic stimulation is shown in Figure 1. The child sat at the center of a drum 3 ft. in diameter. This drum consisted of alternate black and white stripes. It was driven by a motor, which could be run at various constant speeds. Two speeds were employed in this study: 1 and 2 cycles per second, each cycle consisting of a black and white stripe. The drum was rotated clockwise and counterclockwise. These oculomotor responses were also recorded by measuring the corneoretinal potential with the electroencephalogram. Recordings were made first with no instructions. Then the child was asked to fixate the stripes, and the examination was repeated. Head movements were observed continuously throughout the procedure.

Vestibular Examination.—Caloric examination, using cold water, was abandoned after two schizo-

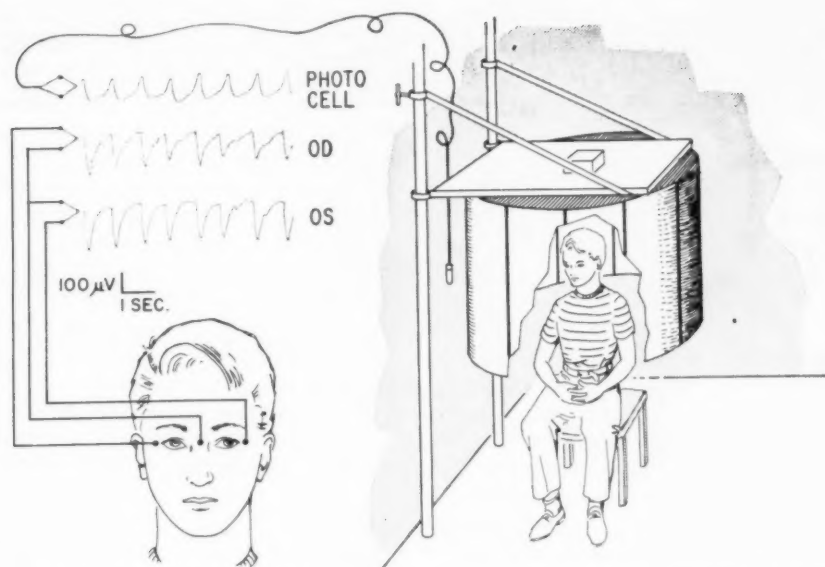


Fig. 1.—The child is seated in the center of the optokinetic drum. Outside the drum there is a photoelectric cell, which is activated by the passage of the white stripes in front of it.

The eye movements are measured by recording changes in the corneoretinal potential with the aid of an electroencephalograph (EEG). The leads are applied at the outer canthi and the bridge of the nose, as indicated, thus recording lateral eye movements. The activity of the photocell is also recorded with the EEG. This technique gives an immediate record of eye movements and correlates them with drum movement. This recording technique also indicates the direction of eye movements. The sample of normal record is arranged, by convention, so that movement to the left is indicated by a downward deflection.

phrenic children proved too uncooperative. However, it was possible to examine the response to rotation in a Bárány chair, employing the usual procedure of 10 revolutions in approximately 20 seconds. First, the child was rotated clockwise and then counterclockwise. If postrotational nystagmus was absent or not sustained on initial rotation, the procedure was repeated. Position of the head and eyes during rotation was noted.

In addition to these oculomotor examinations, we also tested each child's response to passive head turning while standing—the neck righting reflex or "whirling."

Results

No paresis of ocular motility was found in any of the subjects by either direct observation or electrical recording. No child showed evidence of spontaneous nystagmus. Pursuit and command movements, including convergence and divergence, were all intact. In a few of the more disturbed schizophrenic children it was necessary to repeat

the instructions many times in order to elicit a response.

Despite lack of signs of impairment of ocular motility according to these conventional tests, the following deviant oculomotor and vestibular patterns of response were observed: (1) failure to dissociate head and eye movements; (2) involuntary head turning during optokinetic stimulation; (3) diminished or absent nystagmus following Bárány rotation, and (4) head and body rotation ("whirling") on passive head turning. The frequency of occurrence of these abnormal patterns within each of the groups is shown in the accompanying Table.

Failure to Dissociate Head and Eye Movements.—During schematic, command, or pursuit movements to the left or right, the head either turned slightly before the eyes or simultaneously with them in eight of the schizophrenic children and in one

Deviant Oculomotor and Vestibular Responses*

Subject	Age	Head Before Eyes in Light	Head Before Eyes in Dark	Head Rotation During Optokinetic Stimulation	Minimal or Absent Postrotational Nystagmus	Whirling
Schizophrenic Group †						
1	7	—	—	—	—	—
2	7	+	+	N. T.	+	—
3	7	—	—	—	—	—
4	7	—	—	+	—	—
5	7	—	—	—	—	—
6	7	+	+	+	+	+
7	8	+	+	+	+	+
8	8	—	+	+	+	+
9	8	—	+	+	—	—
10	8	+	+	+	N. T.	—
11	8	+	—	—	+	—
12	8	—	—	—	—	—
13	9	+	—	—	+	+
14	9	—	+	+	—	+
15	9	+	+	+	+	+
Totals		8	5	6	7	4
Nonschizophrenic Behavior Disorders ‡						
16	6	—	—	—	—	—
17	7	—	—	—	—	—
18	8	—	—	—	—	—
19	8	+	—	+	+	—
20	8	—	—	—	—	—
21	8	—	—	—	—	—
22	9	—	—	—	—	—
Totals		1	0	1	1	0
Control Group §						
23	3	—	N. T.	N. T.	N. T.	N. T.
24	4	—	—	—	+	—
25	5	—	—	—	—	—
26	6	—	—	—	—	—
27	7	—	—	—	—	—
28	8	—	—	—	—	—
29	8	—	—	—	—	—
30	8	—	—	—	—	—
31	10	—	—	—	—	—
Totals		0	0	0	1	0

* The plus sign (+) indicates abnormal pattern; N. T., not testable.

† Median age 9 yr.

‡ Median age 8 yr.

§ Median age 7 yr.

of the behavior disorder group (Table). This phenomenon was frequently observed in normal children on the initial command to look to one side. However, on subsequent trials, normal children always moved the eyes first, and frequently the head did not move at all.

This inability to dissociate head from eye movement was also witnessed in response to a sudden exposure of a localized flash of light in a dark room in five of the eight schizophrenic children just mentioned. In the normal and clinical controls, the eyes preceded the head (optic righting reflex).

The schizophrenic children who turned the head with the eyes were unable to inhibit the head movement upon request. If the head was restrained, it exerted considerable force in the direction of the eye movements.

Head Turning During Optokinetic Stimulation.—On optokinetic stimulation, involuntary head movement was observed in six schizophrenic children and in one child in the nonschizophrenic behavior disorder group. It was not seen in normal controls. The children who showed this abnormal head movement exhibited no defect in optokinetic nystagmus. However, accompanying the optokinetic nystagmus* there was an involuntary head turning in the direction of the fast component of the nystagmus, i. e., opposite the direction of drum rotation. This lateral deviation was progressive, so that with revolution of the drum the child's head became more displaced from the midline position. It appeared

* Optokinetic nystagmus consists of two phases: (a) a slow eye movement following the stripes in the direction of drum rotation, and (b) a fast movement in the opposite direction.

to be the resultant of a failure to dissociate head movements from eye movement in fixating the oncoming stripes. This abnormal head movement was so marked that after several revolutions of the drum the child's head was in an extreme position of lateral rotation and he was literally looking over his shoulder. This "fencer's" head position could usually be reversed in direction by merely reversing the drum. In two cases (Subjects 10 and 20, Table) the head rotated only to the left.

It is regrettable that our subjects were tested in a sitting position. If they had been tested in a standing position, turning of the body in addition to that of the head might have been elicited and whirling evoked.

Neck Righting Reflex or "Whirling" Phenomenon.—This response was found in four schizophrenic children. They moved their bodies in the direction of head rotation (neck righting reflex). Once started, this movement persisted as long as the examiner's finger remained on the head. If the finger was removed, the child stopped turning. Those who "whirled" also showed involuntary head movements during optokinetic stimulation (Table).

In addition to the whirling response, several of the schizophrenic children and one child with a nonschizophrenic behavior disorder showed abnormal postural responses during Bárány rotation. Thus, Subjects 10, 11, and 20 (Table) could not maintain their balance during rotation, even though they held on to the sides of the chair. One child (Subject 10) almost flew out of the chair during rotation. This inability to remain seated was not seen in the normal children.

Diminished Postrotational Nystagmus.—This response was found in seven of the schizophrenic children and in one child in the behavior disorder group. Following rotation in the Bárány chair, the subject was asked to fixate the examiner's finger. The normal children, with the exception of one 4-year-old, showed brisk, sustained postrotational nystagmus. Diminution or absence of nystagmus was observed in seven of the schizophrenic children. With faster and longer rotation we were still unable to elicit sustained nystagmus in these subjects. Optokinetic nystagmus could not be elicited during Bárány rotation from many of the children who failed to show postrotational nystagmus. Changes in autonomic function

DEVIAANT OCULOMOTOR AND VESTIBULAR RESPONSES

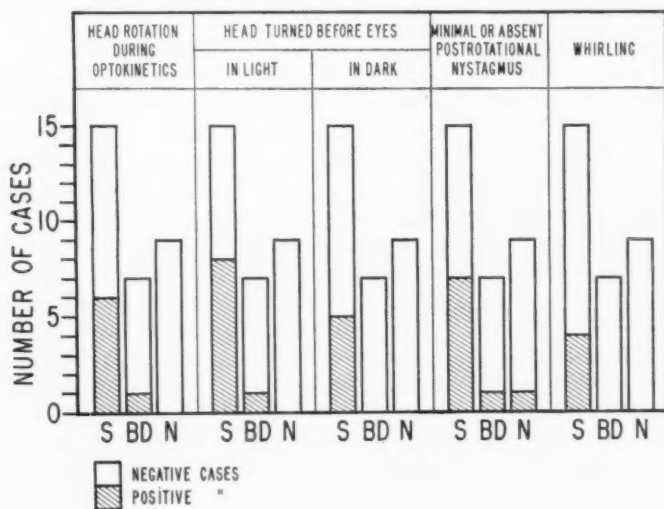


Fig. 2.—Deviant oculomotor and vestibular responses. Bar graphs indicate the number of abnormal responses in each test for the total number of subjects in each diagnostic category: S, schizophrenic; BD, nonschizophrenic behavior disorder; N, normal.

(perspiring, nausea, blanching, flushing, and yawning) during and after rotation were used as indicators of labyrinthine responsiveness.

In summary, 9 of the 15 schizophrenic children showed some form of deviant postural response. In contrast, only one child in the nonschizophrenic behavior disorder group showed any abnormality (Fig. 2). This difference between the schizophrenic group and the other two groups was statistically significant at the 0.01 level of confidence. (The χ^2 -test corrected for discontinuity was employed.)

Minimal or absent postrotational nystagmus was seen in seven of the schizophrenic subjects and in only one of the children in the nonschizophrenic behavior disorder group. In the normal controls of equivalent age, postrotational nystagmus was always present. This difference was also significant at the 0.01 level of confidence.

In spite of the high frequency of abnormality in the schizophrenic group, there were marked individual differences. Six of the schizophrenic children showed no abnormalities of eye, head, or body movements. Their responses were indistinguishable from those of the normal or clinical controls. Furthermore, for each of the procedures there were vast differences in behavior among the schizophrenic children. Thus, during Bárány rotation some of the schizophrenic children became terrified and showed dramatic autonomic and postural changes, while others exhibited no fear of the rotation and enjoyed the procedure.

The schizophrenic children who showed abnormalities in oculomotor and postural functions discussed in this paper also had other neurologic deficits. These were persistent errors on the face-hand test,⁹ instability in tandem walking, and difficulty in performing smooth, rapid alternating and complex movements. The mental examination frequently gave evidence of poor orientation for time and place, poor left-right orientation in regard to the subject's own body, difficulty in carrying out commands

involving crossing of the midline of the subject's own body, and difficulty in simple calculations. The I. Q. scores (Stanford-Binet) of these schizophrenic children, as previously reported,⁹ were subnormal, ranging from 45 to 81. In contrast, those schizophrenic children who did not exhibit any postural abnormalities were within the normal or borderline range with respect to intellectual, perceptual, and motor functioning.

Routine neurologic and electroencephalographic examinations in all the children, including those showing postural abnormalities, were within normal limits.

Comment

The high frequency of deviant postural and righting responses in this group of schizophrenic children, in contrast to the low incidence of such findings among normal children and those with nonschizophrenic behavior disorders, corroborates previous reports.^{2,4,5} Furthermore, they extend our earlier studies,⁹ as well as those of other investigators,^{3,10} in demonstrating that special techniques are needed to elicit neurologic abnormalities in schizophrenic children.

Bender has attributed these abnormal responses to a "maturational lag" in the nervous system and has stressed the role of the tonic neck reflexes and vestibular system in the production of these responses. Such a concept implies an organic dysfunction of the nervous system.

Our observations may be interpreted as indicative of a similar malfunctioning and suggest that Bender's concept of tonic neck reflexes and vestibular dysfunction in the schizophrenic child may be broadened to include disturbances in the oculocephalic reflexes. Perhaps all these defects should be subsumed under the heading of defective righting reflexes. The proof of this concept has yet to be demonstrated. However, there are some observations which, by analogy, appear to bolster this idea. Thus, the only other patients in whom we have observed

head turning during optokinetic stimulation have had severe brain disease, most frequently neoplasms. The inability to dissociate head and eye movements has previously been observed in infants and in adults with organic disease of the brain.¹¹ Contraversion of the head and eyes also appeared but did not persist after subtotal ablation of the human frontal lobe.¹² Such studies imply that circling and transient contraversion of the head and eyes are sensitive signs of disruption of nervous system function and represent, in part, a disturbance of the righting reflexes.

Diminished Nystagmus and Inattention.—The absence or diminution of nystagmus during and after rotation in a Bárány chair suggests another way of analyzing the functional defects observed in this study. Defective rotational nystagmus occurs if the patient does not fixate the environment through which he is turned. Defective postrotational nystagmus has been related to inattention,¹³ to an altered orientation to the external environment,¹⁴ and to a diminution in the use of distant stimuli.¹⁵ Thus, it may be that the reactions to rotation observed in this study reflect an alteration in response to external stimuli.

These concepts receive support from studies on adult schizophrenics which have related indifference, lack of initiative, and poverty of mental content to reduced vestibular responsiveness.¹⁶ Such concepts are also supported by Wendt,¹³ who postulated that loss of postrotational nystagmus occurs when the normal subject fails to remain alert to the external environment. He observed that reduction in responsiveness could be overcome if the subject was kept attentive, and autistic and reverie states were prevented.

The observation that the children with deviant postural responses also exhibited some of the signs of the "organic mental syndrome" suggests that the two sets of phenomena may be related. It also implies that childhood schizophrenics constitute a heterogeneous group, which could be sub-

divided on the basis of their performance in the present study. The validity of such a dichotomy is further suggested by the differences in clinical behavior of these two groups. The schizophrenic children who showed defective postural and oculomotor patterns did not respond to institutional treatment as well as did the other schizophrenic children, and consequently their prognosis was poorer. These findings are consistent with follow-up studies which report a significantly lower incidence of improvement in schizophrenic children with coexistent intellectual retardation.^{17,18}

Perhaps the most significant finding of the present study is that routine neurologic examination is frequently inadequate to demonstrate dysfunction in children diagnosed as schizophrenic, thus pointing to the need for more detailed studies of the neurophysiologic functions in the schizophrenic, brain-damaged, and, above all, normal children.

Summary

Oculomotor (schematic, pursuit, command, and optokinetic nystagmus) and vestibular (rotatory) functions were investigated in 15 institutionalized schizophrenic children, in 7 institutionalized children with nonschizophrenic behavior disorders, and in 9 normal children. Nine of the schizophrenic children, in contrast to only one of the children diagnosed as having a behavior disorder and none of the normal children of equivalent age, showed deviant postural and vestibular reactions. These deviations consisted of involuntary head turning during optokinetic stimulation, inability to dissociate head movement from eye movement, and minimal or absent postrotational nystagmus. Schizophrenic children who showed these abnormalities also showed retardation in perceptual, motor, and intellectual functioning. In addition, they were frequently inattentive and withdrawn. Possible relationships between the deviant

postural reactions and other evidences of neurologic deficits are discussed.

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Responsivity of Adrenal Gland in Schizophrenia to Corticotropin

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Investigations into the function of the adrenal glands in schizophrenia have not yielded uniform results (Altschule¹). The finding of adrenal unresponsiveness by Hoagland et al.⁴ has in general been confirmed by other workers, such as Hemphill and Reiss³ and Faurbye et al.² However, these workers used chronic cases for the most part, in which all physiological changes are difficult to evaluate.

Hoagland et al.⁵ have reported that improvement with EST is correlated with the responsivity of the adrenal cortex, as determined by test injections of corticotropin given to the patient prior to his course of shocks. They found that the more normal the responsivity of the schizophrenic adrenal was to corticotropin the better the subsequent prognosis when the patient was given EST. Pincus and associates⁶ also came to the conclusion there was a relationship between the responsivity of the adrenal cortex and the schizophrenic reaction. Hemphill confirmed these findings to some extent.

The present investigation, therefore, was undertaken to test the following hypotheses:

1. The responsivity of the adrenal cortex to corticotropin is a useful prognostic guide for the treatment of schizophrenia with insulin shock therapy.
2. The responsivity of the adrenal cortex to corticotropin in schizophrenia is correlated with the clinical picture.

Methods

The patients were admitted to the insulin unit at Bethlem Royal Hospital, London. The patients remain in the unit during the course of insulin comas. Treatments are given in the mornings five

days a week, and there is a full program of activities the rest of the time, with a group meeting once a week.

The 24-hour output of 17-ketosteroids, acid-fast formaldehydogenic steroids, and creatinine in the urine were used as indicators of adrenal function. This was with the understanding that, while urinary measures are only a reflection of the compound under investigation, their determination is simpler than determination of blood values. The 24-hour measure was used because of the normal diurnal variation in adrenal gland function. For purposes of comparison, a maximal stimulating dose of corticotropin was used.

The 48-hour corticotropin test was used as being more accurate than the four-hour test.

Day 1: Twenty-four-hour specimen of urine collected.

Day 2: Corticotropin 40 units injected intramuscularly.

Day 3: Corticotropin 40 units injected intramuscularly and a second 24-hour specimen of urine collected.

Both specimens were analyzed for 17-ketosteroids by the method of Robbie and Gibson⁷ with slight modification, and for acid-fast formaldehydogenic steroids by the method of Tompsett.⁸ Although there is dispute as to exactly which compound, i. e., either 17-hydroxysteroids or 17-deoxysteroids, is measured by the method of Tompsett, the technique has the advantage of enabling both of the above determinations to be made from the same extract.

Tests were carried out on 15 patients (11 women and 4 men) but only 6 completed the tests both before and after insulin therapy. Six were tested only before insulin and three only after insulin. In addition, four normal persons were tested.

Results

The results are given in the accompanying Table, in which the figures refer to the difference in output of the compound concerned due to the corticotropin. It can be seen from the Table (Cases 1-6) that there is a lessened responsivity of the adrenal

Response to Injection of Corticotropin (ACTH), in Milligrams per Twenty-Four Hours

Case	Sex	Type	Duration of Symptoms	Corticotropin (ACTH) Response				Clinical Response *
				Before Insulin		After Insulin		
				17-Keto	A. S. F. S.†	17-Keto	A. S. F. S.†	
1	F	Catatonic	1 mo.	30.8	13.5	9.0	0.3	5
2	F	Paranoid	3 mo.	12.0	14.7	-1.4	2.9	3
3	F	Recurrent paranoid	5 yr.	2.2	1.8	-3.8	0.8	2
4	M	Paranoid	1 yr.	10.0	17.1	-2.4	3.0	3
5	M	Paranoid	3 mo.	6.6	9.2	2.4	-2.3	3
6	M	Chronic undiffer.	8 yr.	4.2	-1.55	1.0	-0.5	2
7	F	Acute undiffer.	1 mo.	6.6	0.5	--	--	3
8	F	Paranoid	4 mo.	18.1	13.2	--	--	4
9	F	Paranoid	4 mo.	10.8	23.1	--	--	4
10	M	Paranoid	2 yr.	6.8	0.8	--	--	2
11	F	Paranoid	>5 yr.	5.4	-0.2	--	--	2
12	F	Catatonic	1½ mo.	--	--	-1.6	--	4
13	F	Paranoid	3 mo.	--	--	17	22.5	2
14	F	Catatonic	3 mo.	--	--	3.5	4.1	5
15	F	Catatonic	3 mo.	18.2	5.4	--	--	5
Normals								
A	M			8.6	7.4			
B	M			13.8	3.6			
C	F			14.4	11.3			
D	F			8.2	7.1			

* 1 = worse; 2, no change; 3, slight improvement; 4, moderate improvement, and 5, great improvement; symptom-free.
 † A. S. F. S. = acid-stable formaldehydogenic steroids.

gland after the course of insulin treatment. This applies to men and women and to the 17-ketosteroids, as well as to the "Tompsett" (formaldehydogenic) steroids. This lessened responsivity of the gland is independent of the degree of improvement in the mental picture.

In the second place, it can be seen that the difference in clinical response is related to the pretreatment response to corticotropin, in that the patient showing the greater response to corticotropin shows the greater improvement clinically.

From the Table there would appear to be no specific abnormality in the response of the adrenal glands except that the more acute the psychosis the greater the response of the adrenal gland over the normal values; but the range varies widely in a fashion similar to that of the normal gland. The finding that the more chronic the clinical picture the less responsive the gland was confirmed. In one case (Case 13) where the values were high after treatment, the patient did not improve clinically.

Comment

The significance of these findings is uncertain, as is the interpretation of any physiological changes in schizophrenia, i. e.,

whether they are the result of or are playing a part in the cause of the disease. The adrenal gland is of especial interest, however, because of its intimate role in all antistress reactions. The fact that the adrenocortical hyperactivity disappears later in the disease suggests that its role, if any, is only a precipitating one. Also in favor of this is the fact that no apparent worsening of the clinical picture took place in spite of the increased adrenocortical output caused by the corticotropin.

Although the number of patients used is too small for significant conclusions, the results confirm earlier work in showing that at the end of a course of therapy adrenal function in patients who improve is decreased, but, with one exception (Case 13), show also that the adrenal function decreases even in patients who do not improve. Prognostically, the greater the adrenocortical response to corticotropin before treatment the better the outlook is for insulin therapy. It is felt that these results are sufficient to encourage further work in this area with a view to delimiting the type of acute psychosis which responds best to shock therapies. The test may perhaps be made more differentiating by utilizing submaximal doses of corticotropin, and, finally, it would

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be of interest to perform the same test using differential steroid analysis.

Summary

Fifteen schizophrenic patients were given a 48-hour corticotropin (ACTH) test during a course of insulin therapy. The 24-hour urinary output of 17-ketosteroids and acid-fast formaldehydogenic ("Tompsett") steroids were used as indices. Six patients were tested before and after insulin. Six patients were tested before insulin, and three patients were tested after insulin. Four normal people were also given the 48-hour corticotropin test as a rough comparison. Findings showed that at the end of therapy patients have decreased adrenocortical function independently of improvement. Patients with the greater responses prior to treatment improve to a greater degree.

Dr. D. G. Wilcox and his staff at the clinical laboratory of Bethlem Royal Hospital gave the extensive use of their laboratory facilities.

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Ceruloplasmin, Transferrin, and Tryptophan in Schizophrenia

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It has been suggested that the blood of schizophrenic patients contains a toxic factor which may be the cause of some of the symptoms of the disease.¹ The identity of this compound has not been established. Particularly interesting, however, are the reports which indicate that an indole may be a toxic factor.² There are several theories as to how an unusual indole may arise within the metabolism of the organism. One of the most popular involves the oxidation of epinephrine to some indole-like material.³ Heath's study of the oxidation of epinephrine indicates that this substance is oxidized more rapidly by plasma from schizophrenic persons than by that from normal controls.⁴ Other workers have attempted to show that the copper-containing enzyme, ceruloplasmin, catalyzes this oxidation.⁵ Akerfeldt has measured the rates of oxidation of *N,N'*-dimethyl-*p*-phenylenediamine and reported the results as indicative of ceruloplasmin levels or activities.⁶ Akerfeldt and Abood⁷ both believe that the rate of amine oxidation is higher in schizophrenic patients than in normal controls. From these results they conclude that ceruloplasmin activity is higher in the blood of schizophrenic patients. Such a conclusion may not be well founded, since the oxidation of amines in the body could take place by several different enzymatic processes. In addition to the enzymes involved in the direct oxidation of the amines, other compounds may play a part. One of the most important is ascorbic acid, which is known

to inhibit the Akerfeldt reaction. Thus a low level of ascorbic acid in the blood would increase the rate of oxidation of the aforementioned amines. Since the level of ascorbic acid is often quite low in hospital diets, this fact alone might account for the results reported by Akerfeldt. In view of the inconclusive results from studies of rates of amine oxidation, in order to confirm the suggestion that ceruloplasmin is involved in schizophrenia, it is necessary to prove by some method other than the enzymatic method that abnormal ceruloplasmin levels are present. In this investigation, ceruloplasmin was studied by two methods: a chemical method, in which the copper content of plasma was measured, and an immunological method, in which the ceruloplasmin protein itself was determined. Copper and iron levels are closely associated in blood. Because proteins, to which both elements are bound, are involved in oxidation, it was considered necessary to measure the plasma levels of both iron and transferrin, the iron-containing protein, to see whether any differences existed between normal and schizophrenic subjects.

Another possible source of unusual indoles is the abnormal metabolism of the amino acid tryptophan. Tryptophan is an indole. Abnormal breakdown of this compound may give rise to many unusual indoles. It has been reported that the indole content of urine of schizophrenic patients is quite different from that of normal urine.⁸ It has also been shown that the level of tryptophan is apparently higher in urine of schizophrenic persons than in that of controls.⁹ The levels in urine of trypto-

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phan and related indoles are often quite closely connected with dietary sources. While the rate of tryptophan excretion is not directly proportional to the level of tryptophan in the diet, it has been shown that when subjects are placed on a diet high in animal protein, tryptophan excretion increases.¹⁰ From patients on a low-tryptophan diet, the level of excretion is considerably lower than from patients on a normal diet. Hospital diets are often very different from the diets patients would select of their own accord. The tryptophan content of these diets also may vary. In view of the effect of diet on tryptophan excretion, it was felt wise to repeat this experiment, using patients whose diets had been carefully controlled.

Method

Sixteen patients on carefully controlled diets were used for the copper and iron tests. All these were judged to be schizophrenic. In 11 of the 16 patients the schizophrenic process was chronic; in 5 it was acute. The duration of illness in the former group was in all cases greater than two years. The acute patients had been hospitalized for less than one year. In addition, nine non-schizophrenic patients, with a variety of psychopathologic conditions, were used as in-hospital controls. Three of the inpatient controls were diagnosed as neurotic; three as having manic-depressive psychosis; two as having personality disorders, and one as suffering from an organic brain syndrome. These patients were on the same diet as the patients with schizophrenia. The diets of all inpatient subjects were closely observed; any patient whose diet was considered insufficient was removed from the study. Eleven normal controls from the hospital staff were used in all studies. Twenty-three outpatients at a cancer clinic were used on the transferrin study. These subjects' diets were not controlled. Fasting blood samples were drawn from all subjects. Copper and iron were determined chemically, and ceruloplasmin and transferrin were determined immunologically on the same sample of serum. Copper and iron were determined by the method of Zak.¹¹ To 1.0 ml. of serum, 0.05 ml. of 0.1 N HCl was added, and the sample was heated for five minutes in a near-boiling water bath. The sample was then cooled and 0.4 ml. of 10% trichloroacetic acid added and mixed thoroughly with a clean glass rod. The sample was centrifuged at 3500 rpm for 15 minutes and approximately 10 mg. of solid ascorbic

acid added to the supernatant solution. A 0.5 ml. aliquot was pipetted into a microcuvette, 0.1 ml. of bathocuproine-chlorosulfonic acid reagent added, and the solution mixed. The resulting color was read in a Bausch & Lomb spectrophotometer at 485 m μ wavelength and compared with a curve made from pure copper standards. A second 0.5 ml. aliquot was pipetted into a microcuvette for iron determination. To this, 0.1 ml. of the bathophenanthroline-chlorosulfonic acid reagent was added, and the solutions mixed and read in the spectrophotometer at 535 m μ .

Copper Reagent

To 100 mg. of bathocuproine was added 0.4 ml. of iron-free chlorosulfonic acid. The mixture was heated over a microburner for 30 seconds. After cooling, 10.0 ml. of contaminant-free distilled water was added and the solution warmed in a water bath with stirring to dissolve all solid material. Three ml. of this solution was diluted to 100.0 ml. with 45% sodium acetate, filtered, and stored in glass-stoppered brown bottles.

Iron Reagent

To 100 mg. of bathophenanthroline was added 0.5 ml. of iron-free chlorosulfonic acid. The resulting mixture was heated over a microburner for 20 seconds. It was cooled, and 10.0 ml. of contaminant-free distilled water was added. The resulting solution was warmed in a water bath to dissolve all solid material. Three-tenths milliliter of this solution was diluted to 100.0 ml. with 45% sodium acetate solution. Any insoluble material was filtered off, and this solution was stored in glass-stoppered brown bottles.

Immunochemical Method

The ceruloplasmin and transferrin levels were determined immunologically by the method of Goodman et al.¹²⁻¹⁶ For the ceruloplasmin determination, to 0.1 ml. of serum was added 0.9 cc. of sodium chloride solution of sufficient concentration to give a final concentration of 13%. For the transferrin determination, to 0.1 ml. of serum was added 4.9 ml. of sodium chloride solution to bring the NaCl concentration to the same point. Two-tenths milliliter of diluted serum was then added to 0.3 ml. of the antiserum preparation. After this, these solutions were mixed and then immediately incubated at 38 C for one hour. At the same time a blank, consisting of 0.2 ml. of 13% saline and 0.3 ml. of antiserum, was incubated. The absorption of samples was then determined at 450 m μ in a Bausch & Lomb spectrophotometer. The results were then obtained from a standard curve. A control, consisting of 0.2 ml. of diluted

TABLE 1.—*Cooper and Ceruloplasmin Levels in Serum of Schizophrenic and Nonschizophrenic Subjects*

	N	Copper		Ceruloplasmin	
		Mean γ %	S. D.	Mean Mg. %	S. D.
Schizophrenic patients	16	116.5	12.3	38.08	5.05
Normal controls	11	112.5	27.0	35.91	8.52
Nonschizophrenic patients	9	131.1	32.2	42.46	8.49

serum and 0.3 ml. of 13% saline solution, was read and subtracted from the reading of the sample to correct for serum turbidity.

The subjects of the tryptophan experiment were studied for three days on a normal hospital diet, two days on a high-tryptophan diet, and five days on a low-tryptophan diet. The urinary tryptophans were determined by the method of Hopkins Cole.¹⁴ The method is only semiquantitative, but it was felt that the same method as that used in the original study should be used to check any differences observed from the previous results. Tests were graded as —, +1, +2, +3, or +4, depending on the intensity of the ring. Analysis of variance was used to determine all levels of significance.¹⁵ The *P* values reported refer to the probability that the observed differences could be attributed to chance factors.

Results and Comment

The levels of copper and ceruloplasmin in the serum of the three groups are shown in Table 1. There were no significant differences among the groups in either study. These results suggest that normal and schizophrenic subjects do not differ with respect to copper or ceruloplasmin levels. It still remains to be shown that no qualitative differences exist between ceruloplasmin or copper levels in the various groups. Some slight difference among the groups could possibly exist in either the structure or the oxidative activity of the ceruloplasmin.

Results of the determination of the iron and transferrin levels in the serum of the three groups are shown in Table 2. The iron levels of the schizophrenic group differed from those of the normal group; these results were significant at the 0.05 level. There was, however, no significant difference between the schizophrenic inpatients and the group of inpatients with other

mental disorders. It may be assumed, then, that the difference in serum iron level between schizophrenic inpatients and normal subjects may be the result of either hospital diet or hospital regime, rather than a characteristic of schizophrenia.

The levels of transferrin in the serum differed significantly among the four groups ($P < 0.005$). The schizophrenic group was lower than the normal, nonhospitalized group ($P < 0.10$). The schizophrenic inpatients and other inpatients did not differ significantly. Again, it must be concluded that the observed difference could be due either to hospital diet or to hospital regime rather than to specific characteristics of any particular disease. The significance of lowered levels of various serum proteins is still not well understood. The lowering of the transferrin level could well be a result of a general mechanism triggered by disease, instead of one caused by diet. Indeed, in cancer there was an even greater drop in transferrin levels; the difference between the normal and the cancer group was significant at the 0.001 level. A further survey of the levels of this protein in other disease states is necessary to help determine the cause of the drop.

The results of the tryptophan study are shown in Table 3. There was no significant difference between excretion of tryptophan by schizophrenic and by nonschizophrenic inpatients. When the amount of tryptophan in the diet was increased, all subjects increased their rate of tryptophan excretion significantly ($P < 0.005$). When the amount of tryptophan in the diet was decreased, the excretion of tryptophan was lowered in

TABLE 2.—*Iron and Transferrin Levels in Serum of Schizophrenic and Nonschizophrenic Subjects*

	N	Iron		Transferrin	
		Mean γ %	S. D.	Mean Mg. %	S. D.
Schizophrenic patients	16	141.8	50.7	220.4	47.4
Normal controls	11	195.5	36.9	265.5	58.1
Nonschizophrenic patients	9	124.4	33.9	215.6	34.0
Cancer patients	23	—	—	197.5	44.8

CERULOPLASMIN, TRANSFERRIN, AND TRYPTOPHAN

TABLE 3.—Tryptophan Excretions of Patients on Various Diets

Group		High	Normal	Low	Subject Mean
Schizophrenic	{ N	3	3	3	3
	{ Mean	2.60	1.43	0.67	1.57
	{ S. D.	1.34	0.84	0.60	0.90
Normal patient	{ N	4	4	4	4
	{ Mean	3.25	1.48	1.50	2.08
	{ S. D.	0.56	0.76	0.24	0.11
Total	{ N	7	7	7	7
	{ Mean	2.97	1.46	1.14	1.86
	{ S. D.	1.02	0.80	0.60	0.65

both groups, although not significantly. It must be concluded that the level of tryptophan excretion is a result of diet rather than of a defect present in schizophrenia. Correlations among the various measures are given in Table 4. It is recognized that the number of cases involved is quite small for correlation purposes, but the results are reported here, since they may be of interest to other investigators. In one instance, the correlation between copper and ceruloplasmin, the correlation of +0.366 for the schizophrenic group is significantly different ($P < 0.05$) from the correlation of +0.799 for the normal plus nonschizophrenic groups combined.

Summary

Thorough investigation of copper and ceruloplasmin levels in normal and schizophrenic subjects gave no indication that these substances are altered quantitatively in schizophrenia. It remains to be shown whether or not qualitative differences exist

in this disease. The same study of iron and transferrin levels shows that, while schizophrenic subjects have lowered quantities of these substances, the levels in the other patients studied were lowered as much or more. Investigation of tryptophan excretion of normal and schizophrenic subjects on normal-, high-, and low-tryptophan diets gave no indication that increased tryptophan excretion was associated with schizophrenia. The findings give clear evidence that diet must be rigidly controlled before metabolic investigations can be considered to be of significance.

Addendum

As further proof that ceruloplasmin levels are not elevated in schizophrenia it should be mentioned that Scheinberg and co-workers failed to find a significant elevation of ceruloplasmin enzymatic activity in schizophrenic patients (Scheinberg, I. H.; Morell, A. G.; Harris, R. S., and Berger, A.: Concentration of Ceruloplasmin in Plasma of Schizophrenic Patients, *Science* 126:925, 1957).

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TABLE 4.—Intercorrelations Among Variables

		Ceruloplasmin		Iron		Transferrin	
		N	r	N	r	N	r
Copper	Normal	11	+0.815 *	11	-0.689 †	11	-0.050
	Nonschizophrenic	8	+0.769 †	8	+0.189	9	-0.141
	Schizophrenic	16	+0.366	11	-0.052	16	-0.244
	Total	35	+0.716 *	30	-0.213	36	-0.187
Ceruloplasmin	Normal			11	-0.564	11	+0.079
	Nonschizophrenic			7	-0.214	8	-0.496
	Schizophrenic			11	+0.076	16	+0.065
	Total			29	-0.334	35	-0.140
Iron	Normal					11	-0.269
	Nonschizophrenic					8	+0.444
	Schizophrenic					11	-0.340
	Total					30	+0.140

* r is significantly different from zero at the 0.01 level.

† r is significantly different from zero at the 0.05 level.

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BOOK REVIEWS

The Annual Survey of Psychoanalysis. Edited by John Frosch, M.D., and Nathaniel Ross, M.D. Price, \$12.00. Pp. 770. International Universities Press, Inc., 227 W. 13th St., New York 11, 1957.

This fourth volume of "The Annual Survey of Psychoanalysis" encompasses the published work during 1953. The literature is most adequately covered, including the presentation of the important books of the year and not only the psychoanalytic articles themselves but also much in the way of related material. The bibliography includes 258 items listed separately at the end of the volume, following which there is an extremely adequate index. The material is abstracted under a number of headings, including History, Critique and Methodology, Critique of Specific Contributions or Contributors, Ego Psychology and Instinct Studies, Clinical Studies, Dream Studies, Psychoanalytic Child Psychiatry, Applied Psychoanalysis, Psychoanalytic Therapy, Psychoanalytic Training, Psychoanalytic Studies in Psychiatry, and, finally, Psychoanalytic Books.

As has been stated in a previous review, this volume presents the psychoanalytic literature for the year 1953 in style and form much more suitable for understanding than the original articles. The abstracts are well written and contain most of the pertinent material, without much of the extraneous and unnecessary material within the actual papers.

The reviewer congratulates the editors and their associates on performing a most valuable service for the field of psychiatry in general and of psychoanalysis in particular. One wonders how long these editors can continue such a time-consuming and arduous task. Hopefully, they will find a continually interested group of colleagues to help them and to take over when they become fatigued.

ROY R. GRINKER, M.D.

The Caricature of Love. By Hervey M. Cleckley. Price, \$6.50. Pp. 319. The Ronald Press Company, 15 E. 26th St., New York 10, 1957.

In this book, Dr. Cleckley appears to have summoned considerable literary talent, erudition, and intense personal conviction in a diatribe against homosexual influences in our culture and the Freudian doctrines that he believes support these influences. The book, though repetitious, lacking in integration, and axe-grinding throughout, is worthy of review for its loose but cyclopedic collection of homosexual allusions in the literature and its provocative thesis that subversive homosexual influences are a threatening fact of modern times.

Questions raised and answered by the author include whether homosexuality is pathological and whether we should be alarmed about its incidence in our society and its alleged promulgation by such things as the Kinsey report, Gide's citation by the Nobel Prize Committee, and the popularity of Freudian psychiatry. He concerns himself in one chapter with the subtle propaganda the public is exposed to by the high percentage of homosexual persons in the movie industry who might be clearly, but nonovertly, pervading their productions with arguments in favor of homosexual versus heterosexual love. He is less concerned with Gide and others (such as Wylie), who are more openly advocating homosexual experience. His attitude toward these latter authors fluctuates, however, as it appears to toward homosexuals themselves, from a sympathetic pity to a frank rejection of their worthiness in the literary area. Dr. Cleckley frequently mentions his lack of qualification to judge the literary merits of authors who either are known homosexuals or are writing overt or covert homosexual material, fictional or non-fictional. He purports to focus only on the issue of their influence in our society. One is left with the impression, however, that he would like to suppress their writings as undermining the moral fabric of Western civilization, in leading us, like the Pied Piper, to our destruction.

The first half of the book is largely concerned with the author's frank distaste of and disbelief in most Freudian hypotheses, particularly the concept of bisexuality and universal latent homosexuality. Here the book is reminiscent of other recent monographs denouncing Freud and his theories as unscientific, immoral, etc. This portion of the book is particularly dull, repetitious, and difficult to find engrossing. One is puzzled by Dr. Cleckley's seeming unaware-

ness of unconscious processes versus conscious ones. For example, his argument that the typical prepubertal and pubertal preference for the companionship of one's own sex does not in any way reflect homosexual trends seems naive in the extreme. On the other hand, there is some value in his reminding us of the need for clearer concepts and less use of analytic jargon. Early in the book the author seizes on a letter Freud wrote to a woman in America about her homosexual son, and, with utter disregard for the framework of its origin and the fact that it was not a professional publication of Freud, uses it as Freud's official and final view on the subject of homosexuality. He repeatedly refers back to the letter as proof that Freud—and his followers—take the position that homosexuality is normal. On the other hand, Cleckley quotes certain analysts in whose writings he finds support, and tells us that his real complaint is only that analytic doctrine can be a bad thing in the hands of the lay public, who are likely to misunderstand it. He states: "Valuable as these methods [inductive analytic] may be, at present they obviously have an intrinsic and peculiar potentiality for misuse." This is a doubtful position, judging by his over-all panning of the doctrines themselves. Dr. Cleckley's preoccupation with "normality" and his denial of the continuum between normal psychology and psychopathology are likely to leave contemporary psychiatrists, analytic and nonanalytic alike, somewhat astonished. Sincere though he may be, Dr. Cleckley appears to have at least fallen into the same trap he professes to be concerned about in the book—that of professional people propagandizing and misleading the laity about psychiatric knowledge and points of view.

The more interesting, but less reviewable, portion of the book concerns the personal lives and writings of various authors who either are themselves known homosexuals, or wrote overtly or covertly in a way to encourage or condone homosexuality. These include Gide, Swinburne, Strindberg, Lawrence, Wilde, Philip Wylie, Beaudelaire, and Plato. As stated earlier, he is less concerned with overt homosexual writings, such as some of Gide's, than with the issue of a subtle influence in favor of a homosexual orientation, including such things as the Kinsey report. Leaving aside the accuracy of Dr. Cleckley's information about these men of genius, his interpretation of their writings is at times debatable, and his axe-grinding seldom ceases, though it is less leaden and repetitious than in the first half of the book.

In summary, this book is interesting reading because of its provocative point of view about the evil influence of certain literary influences on our culture. It supports the idea that we are being exposed to an increasing barrage of prohomosexual influences from this source, encouraged by the widespread misuse of psychoanalytic theory.

GEORGE H. ALLISIN, M.D.

The Neuroses and Their Treatment. Edited by Edward Podolsky, M.D. Price, \$10.00. Pp. 555. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1958.

Dr. Podolsky has selected some forty papers which he terms representative, containing the latest knowledge of specialists in the handling of the neuroses. This is not a textbook, but a compilation of papers already written and for the most part published by the chosen authors. They range all the way from psychoanalytic therapy of a neurotic child to carbon dioxide inhalations, as presented by Meduna. In addition, there are a number of theoretical papers devoted to the discussion of evaluation of psychotherapy and some experimental studies, such as the work of Holmes and Ripley. Each individual author writes in his own style, with varying degrees of profundity. The papers are, naturally, uneven in their value. Some are apparently quite hastily put together from previous work and show no inner consistency. The book itself has no bibliography, and each chapter lacks references of cited work, with few exceptions. There is no index to the book. Sometimes it is valuable for the student and the beginner in the field to have available a collection of classical and significant papers, so that he does not have to go through the literature himself and is saved the trouble of library research. However, this volume does not contain the necessary material which would give a good overview of the neuroses and their treatment. The content and form of presentation of the papers within this compilation leave much to be desired.

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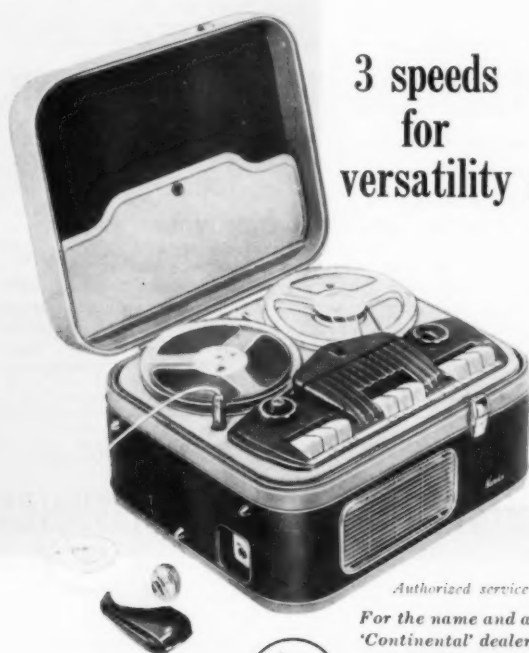


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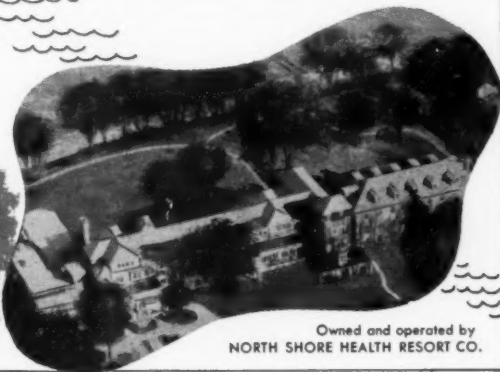
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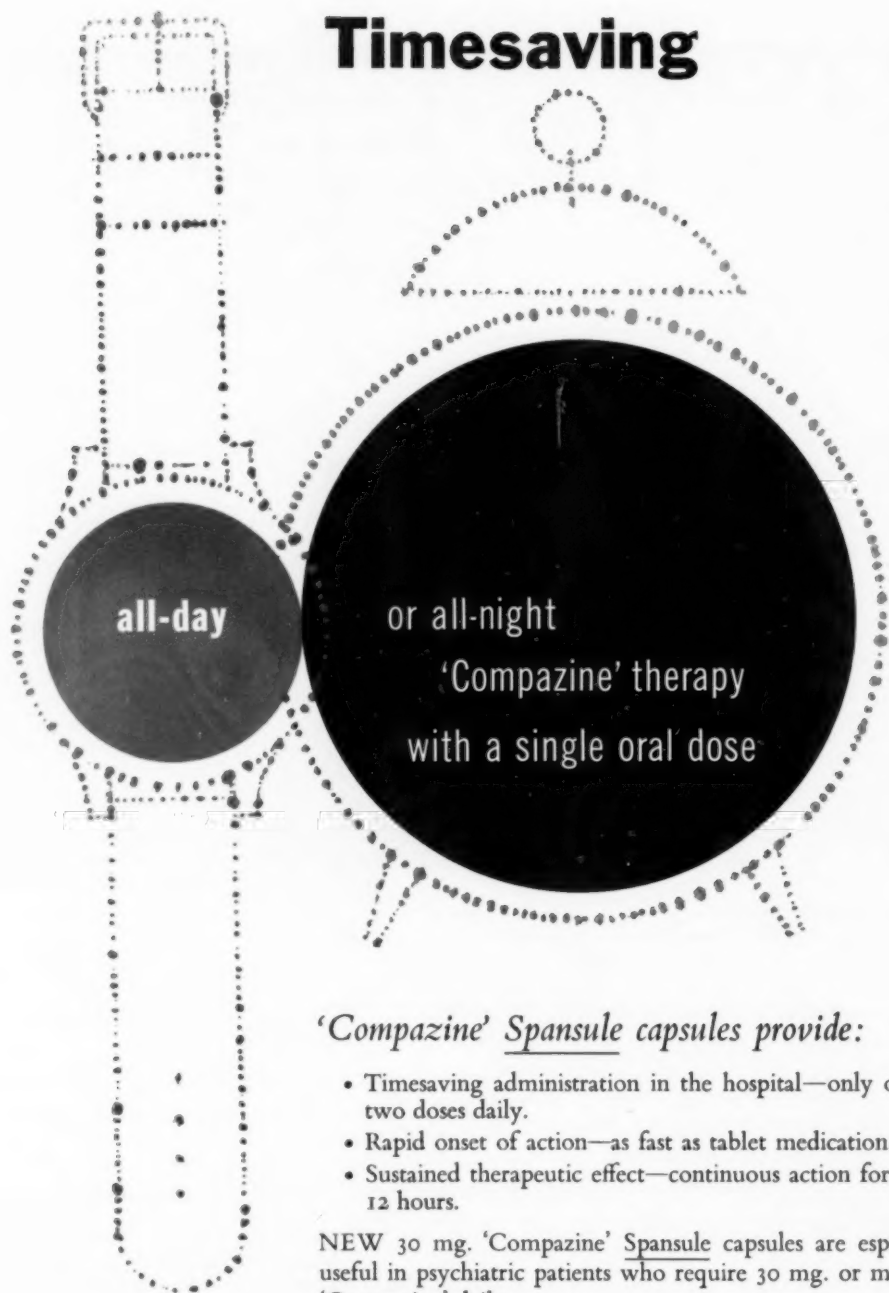
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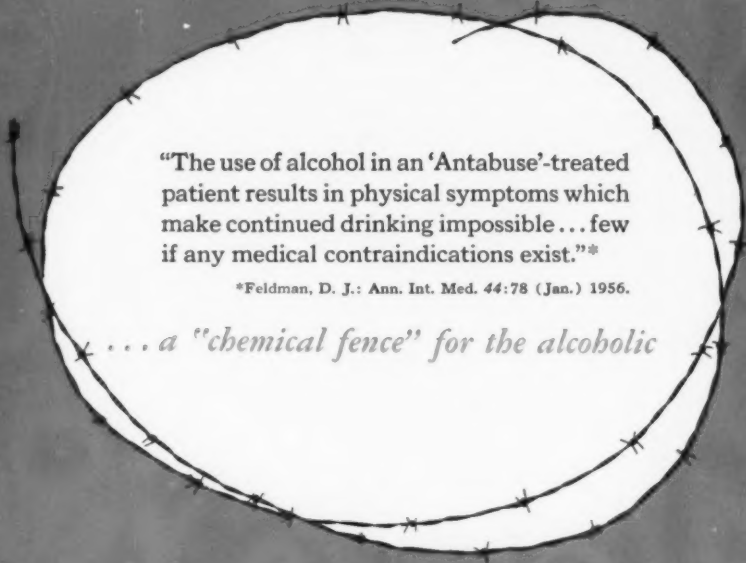
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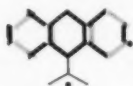
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